06 Human physiology

Artwork showing fertilization. Three sperm are shown, but only one will fertilize the ovum.

Essential ideas

6.1	The structure of the wall of the small intestine allows it to move, digest, and absorb food.
6.2	The blood system continuously transports substances to cells and simultaneously collects waste products.
6.3	The human body has structures and processes that resist the continuous threat of invasion by pathogens.
6.4	The lungs are actively ventilated to ensure that gas exchange can occur passively.
6.5	Neurones transmit the message, synapses modulate the message.
6.6	Hormones are used when signals need to be widely distributed.

The human body is composed of cells organized into tissues, tissues organized into organs, and organs organized into organ systems. The anatomy and physiology of the human body is so complex that researchers will be investigating it for many decades to come. In this chapter, you will learn about the physiology of some of the major organ systems of the body, and how those organ systems interact with each other. The science of anatomy is based on identifying structures and parts of structures. The focus of our study will be physiology, which is how the various organs and tissues within your body function. It is a fascinating story.

6.1 Digestion and absorption

NATURE OF SCIENCE

Use models as representations of the real world: dialysis tubing can be used to model absorption in the intestine.

Understandings:

- The contraction of circular and longitudinal muscle of the small intestine mixes the food with enzymes and moves it along the gut.
- The pancreas secretes enzymes into the lumen of the small intestine.
- Enzymes digest most macromolecules in food into monomers in the small intestine.
- Villi increase the surface area of epithelium over which absorption is carried out.
- Villi absorb monomers formed by digestion as well as mineral ions and vitamins.
- Different methods of membrane transport are required to absorb different nutrients.

Applications and skills:

- Application: Processes occurring in the small intestine that result in the digestion of starch and transport of the products of digestion to the liver.
- Application: Use of dialysis tubing to model absorption of digested food in the intestine.
- Skill: Production of an annotated diagram of the digestive system.
- Skill: Identification of tissue layers in transverse sections of the small intestine viewed with a microscope or in a micrograph.

Guidance

- *Students should know that amylase, lipase, and an endopeptidase are secreted by the pancreas. The name trypsin and the method used to activate it are not required.*
- *Students should know that starch, glycogen, lipids, and nucleic acids are digested into monomers, and that cellulose remains undigested.*
- *Tissue layers should include longitudinal and circular muscles, mucosa and epithelium.*

An artist's drawing of the ventral view of a healthy digestive system.

Digestion is an enzyme-facilitated chemical process

When you eat a snack or meal, a series of events is begun that leads to your body cells being provided with the nutrients that they need. Put very simply, the order of events is:

- ingestion – you eat the food
- digestion – a series of chemical reactions occurs, whereby the ingested food is converted into smaller and smaller molecular forms
- absorption – small molecular forms are absorbed through the cells of your digestive system and pass into nearby blood or lymphatic vessels
- transport – your circulatory system delivers the small molecular nutrients to your body cells.

Many of the foods we ingest have very large molecules that are too large to pass across any cell membrane. Yet to get into our bloodstream, molecules must pass through the cell membranes of our intestines and then through the cell membrane of a capillary vessel. Therefore any food that we eat must be chemically digested to a suitable size. Table 6.1 shows different types of molecules found in food and their molecular form before and after digestion.

Table 6.1 Food molecules

Molecule type	Molecular form ingested	Molecular form after digestion
Proteins	Proteins	Amino acids
Lipids	Triglycerides	Glycerol and fatty acids
Carbohydrates	Polysaccharides, disaccharides, monosaccharides	Monosaccharides
Nucleic acids	DNA, RNA	Nucleotides

When we digest food molecules, we hydrolyse them into their smallest components (as shown in the right-hand column of Table 6.1). The components can then be reassembled into larger molecules (macromolecules) that are useful to our bodies.

Humans are incapable of digesting cellulose, one of the most common organic substances on Earth. In fact very few living organisms are capable of digesting cellulose, because they can't produce the enzyme cellulase.

Role of enzymes during digestion

As food moves through your alimentary canal, many digestive enzymes are added to it along the way. Each digestive enzyme is specific for a specific food type. For example, lipase is an enzyme specific for lipid molecules, and amylase is specific for amylose (otherwise known as starch). As you may remember, enzymes are protein molecules that act as catalysts for reactions. As catalysts, the function of enzymes is to lower the activation energy of the reactions that they catalyse. This means that reactions taking place with an enzyme can occur with a lower input of energy than the same reaction

taking place without the presence of an enzyme. The input of energy is typically in the form of heat. Enzyme-catalysed reactions proceed at higher reaction rates at a lower temperature than the same reaction without an enzyme. The reactions of digestion are all very similar because they are all hydrolysis reactions.

Humans maintain a stable body temperature of 37°C. This temperature is warm enough to maintain a good molecular movement and, with the aid of enzymes, it provides enough activation energy for metabolic reactions to occur, including digestion.

Warm-blooded organisms such as humans have an advantage over cold-blooded organisms for efficient digestion and many other metabolic processes, because of their constantly warm internal temperature. However, we would not be able to obtain sufficient nutrients from ingested foods without the aid of digestive enzymes.

Some digested molecules are absorbed into a system of your body called the lymphatic system. This is particularly true of fatty acids because of their non-polarity and relatively large molecular size.

The anatomy of the human digestive system

The human digestive system is fundamentally a long tube called the alimentary canal with two accessory organs (the pancreas and liver) that are connected by ducts into the canal. The alimentary canal begins with the mouth and ends with the anus. Any solids or liquids that you ingest are either, after digestion, absorbed into the bloodstream or, if not absorbed, eliminated as faeces.

The human digestive system shown in Figure 6.1 has been simplified so that you can use it as a basis for practising drawing and labelling the digestive system. The lungs are shown to give some perspective to the location of the thoracic cavity, which contains the heart and lungs, compared with the abdominal cavity, which contains all of the digestive structures shown apart from the mouth and oesophagus.

Make sure you practise the drawings that you will be expected to be able to produce in an exam. Adding labels to an existing diagram is relatively easy compared with starting from a blank piece of paper and producing an entire diagram with labels and/or annotated functions.

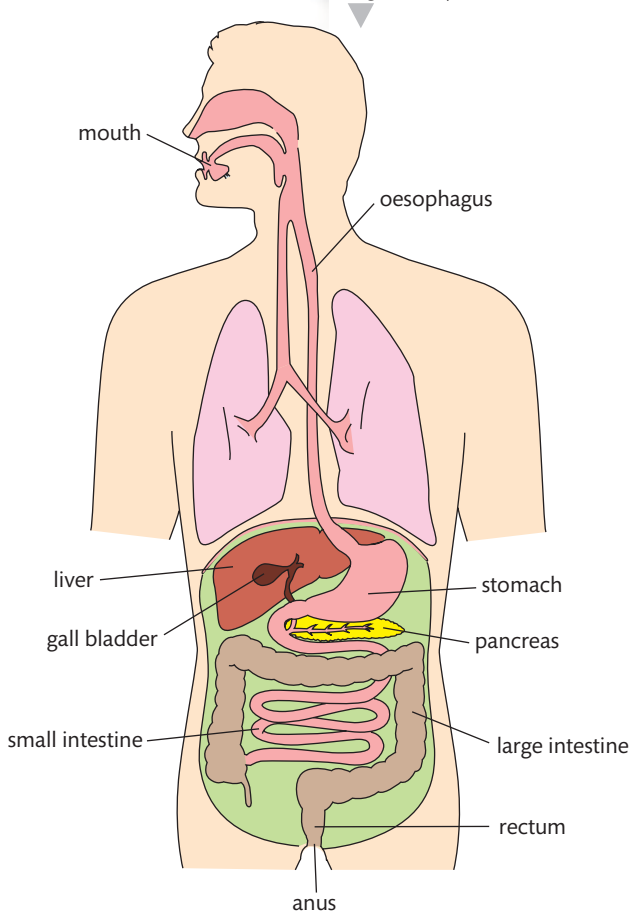


Figure 6.1 The human digestive system.

The alimentary canal is a muscular tube

Food does not make its one-way journey through the alimentary canal by gravity. Indeed, food material often has to move against gravity. So, what keeps food moving, and moving in the one direction? The answer is muscles, specifically smooth muscles. Smooth muscle is controlled by the autonomic nervous system (ANS), and you are not aware that your smooth muscle is contracting. The tube of the alimentary canal has two layers of smooth muscle, called circular and longitudinal. A simplified drawing of these two layers is shown in Figure 6.2. The contracting fibres of the inner, circular, muscles do indeed make a 'circle', as shown in this section, while the contracting fibres of the longitudinal muscles are positioned at right angles to the circular muscles. The muscle motion and food movement caused by the action of these two muscle layers is called peristalsis.

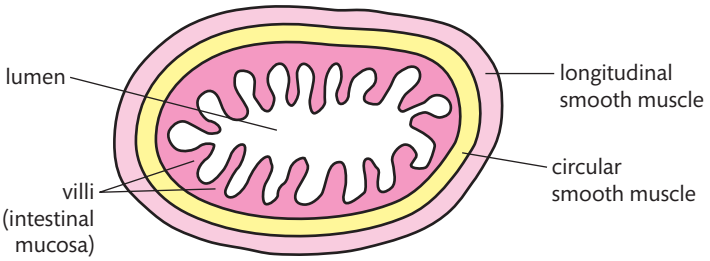
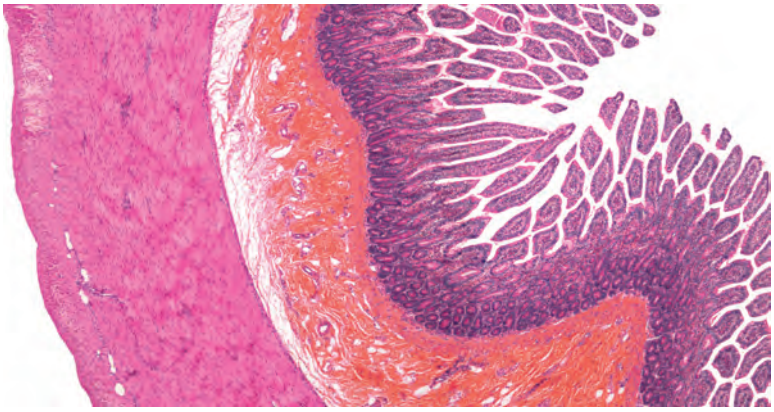


Figure 6.2 This simplified drawing shows a section of the small intestine showing the relative locations of the circular and longitudinal muscles. The same arrangement would also be found in the oesophagus, stomach, and large intestine. The only part of this sketch that is specific to the small intestine is the villi, used for absorption.



A light microscope photograph showing a small area of the small intestine. The white area in the upper right corner is the lumen (cavity) of the intestine, where unabsorbed food would be located. To the lower left of that are the villi, which are used for absorption. Further left are the circular and longitudinal muscle layers used for peristalsis.

Peristalsis is used in the stomach to mix food with digestive secretions, including a protein-digesting enzyme. This movement is called churning. In the rest of the alimentary canal, peristalsis causes a contraction just 'behind' the food mass and thus keeps it moving through the canal, as well as helping to mix the food with a variety of enzymes. The peristaltic movement is relatively fast within the oesophagus and slows dramatically in the intestines.

A person who is hanging upside down can still swallow food and the food will travel 'up' to the stomach. This is because the food is moved by peristalsis, not by gravity.

The role of the pancreas during digestion

The pancreas is a multipurpose organ. In addition to producing two important hormones (insulin and glucagon) involved in glucose metabolism, the pancreas produces three enzymes involved in digestion: lipase, amylase, and a protein-digesting enzyme known as an endopeptidase. Those three enzymes are part of a fluid known simply as pancreatic juice that is released into the first portion of the small intestine through a duct. Look closely at the artwork opposite and you will see the pancreatic duct. The duct allows the three enzymes to enter the lumen (cavity) of the small intestine, where partially digested food from the stomach is being released.

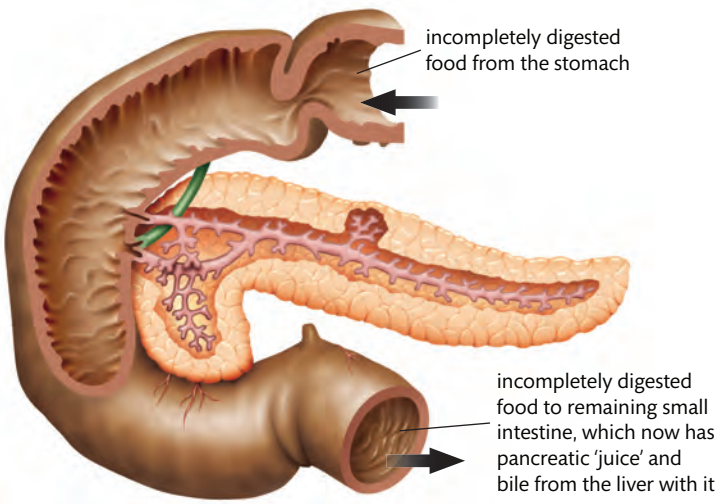
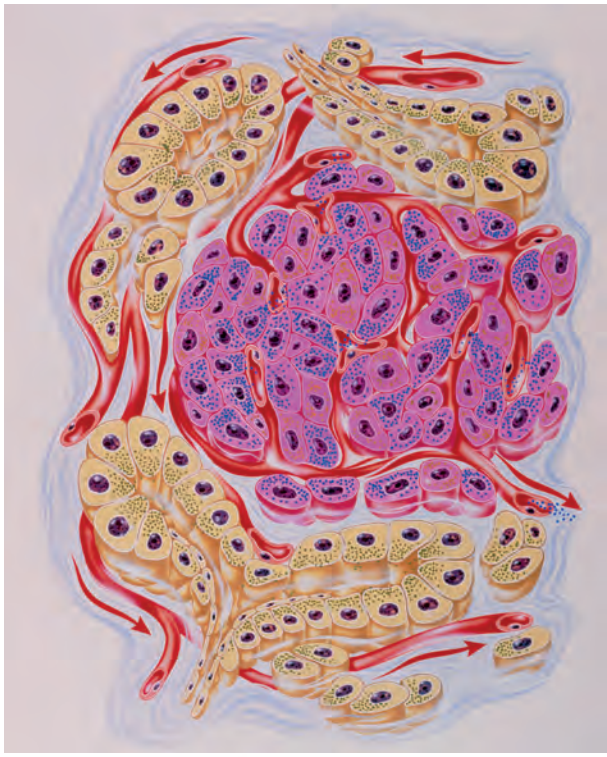


Figure 6.3 Artwork showing the pancreas and pancreatic ducts leading to the lumen of the first section of the small intestine. The green tube shown is bringing bile from the liver (not shown) to be added to aid lipid digestion. The area at the top that is cut is where the stomach is located, and the lower area that is cut is where the very long small intestine continues.

Table 6.2 Digestive enzymes produced by the pancreas and secreted into the lumen of the small intestine

Enzyme	Substrate	Action
Lipase	Lipids (fats and oils)	Hydrolyses lipids into glycerol and fatty acids
Amylase	Starch	Hydrolyses starch into the disaccharide maltose. Another enzyme then hydrolyses maltose into glucose
Trypsin (an endopeptidase)	Proteins (polypeptides)	An endopeptidase hydrolyses long polypeptides into smaller polypeptides. Further protein-digesting enzymes then hydrolyse the smaller polypeptides into amino acids



This illustration shows the cells that are involved in two major aspects of pancreatic function. The brightly coloured cells are endocrine (hormone-producing cells), which produce hormones that are then transported away by the bloodstream. The yellow-coloured cells are cells that produce digestive enzymes that are released into very small ducts (look closely at the lower left of the picture) that eventually join into the pancreatic duct that leads to the small intestine.

The role of the small intestine in digestion and absorption

As an example of what happens as ingested foods move through the small intestine, let's see how starch is digested and how its monomers are absorbed.

The chemical digestion of starch begins in the mouth, with the addition of saliva to the food. Saliva contains amylase, the enzyme that hydrolyses the starch polysaccharide into the disaccharide maltose. The hydrolytic activity of amylase ceases in the highly acidic environment of the stomach. Therefore, the starch remains largely undigested when the contents of the stomach are released into the small intestine.

As described earlier, the pancreas produces and secretes pancreatic juice, and sends that juice into the first section of the small intestine, which is called the duodenum. One of the components of pancreatic juice is amylase. The pH environment of the small intestine is neutral to slightly alkaline, which is the optimum pH for amylase. Thus the amylase molecules begin to catalyse the hydrolysis of starch to maltose. As peristalsis continues to move the food through the lumen of the small intestine, the hydrolytic reactions continue.

Within the small intestine there is another enzyme that completes the digestion of starch. The enzyme maltase catalyses the hydrolysis of maltose into two molecules of glucose. Maltase is produced by the cells of the inner lining of the small intestine, and typically remains bound into the plasma membranes of the epithelial cells that are in contact with the food material within the lumen.

Absorption of glucose into villi

The cells in the inner lining of the small intestine make up what is called the mucosa. The mucosa has many small folds or projections called villi (singular villus). Each villus is composed of many cells whose primary job is selectively absorbing molecules found in the lumen of the small intestine. The actual absorption occurs through cells in an epithelial layer that is in direct contact with the nutrients. The epithelial cells have tiny

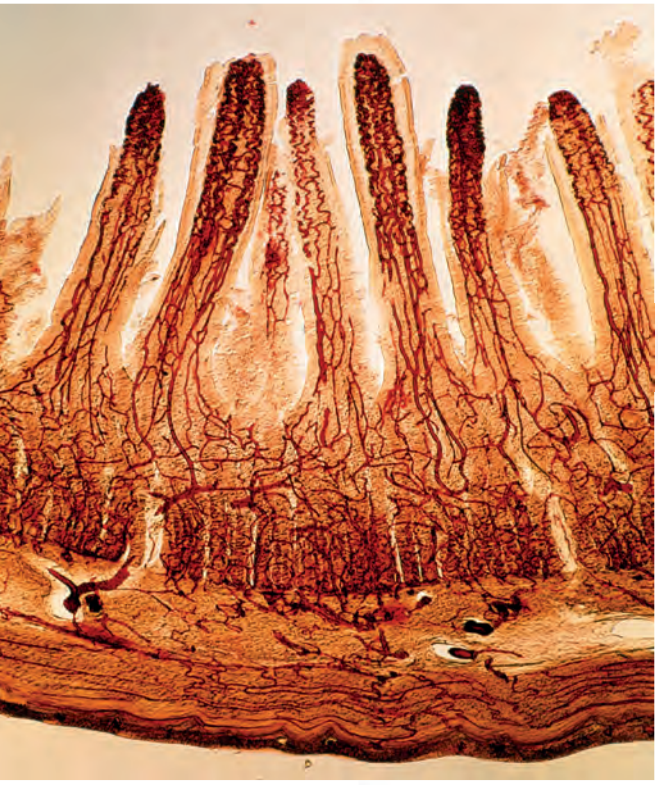
The hydrolytic enzyme lactase is being extracted commercially from certain yeasts, and is being used to hydrolyse the disaccharide lactose from milk and milk products. This is especially helpful for people who are lactose intolerant.

membrane projections called microvilli that extend into the lumen of the intestine. The villi and microvilli greatly increase the surface area for absorption within the small intestine, compared with a smooth-walled structure. The interior of each villus contains a capillary bed for nutrient absorption and transport of digested monomers by the bloodstream. In addition, there is a small vessel of the lymphatic system present, called a lacteal, that absorbs some of the nutrients. After passing through the epithelial cells of a villus, most monomers are absorbed into the inner capillary bed. However, some of the larger monomers, such as fatty acids, are absorbed first into a lacteal.

Here is a partial list of the substances absorbed through villi into the bloodstream or lymph fluid:

- water
- glucose (plus other monosaccharides)
- amino acids
- nucleotides
- glycerol
- fatty acids
- mineral ions
- vitamins.

A light microscope photograph showing a transverse section through several villi. Microvilli are too small to be seen at this magnification. The capillary bed inside each villus is clearly visible. The longitudinal and circular muscles of the wall of the intestine are also visible at the bottom of the photograph.



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Each country has its own laws concerning how food is labelled for consumers. Some countries require detailed lists of important information, such as fat content, fat type, calories per serving, etc., while other countries have no requirements at all. Do all the citizens of a country have a right to know the contents of the food that they are buying?

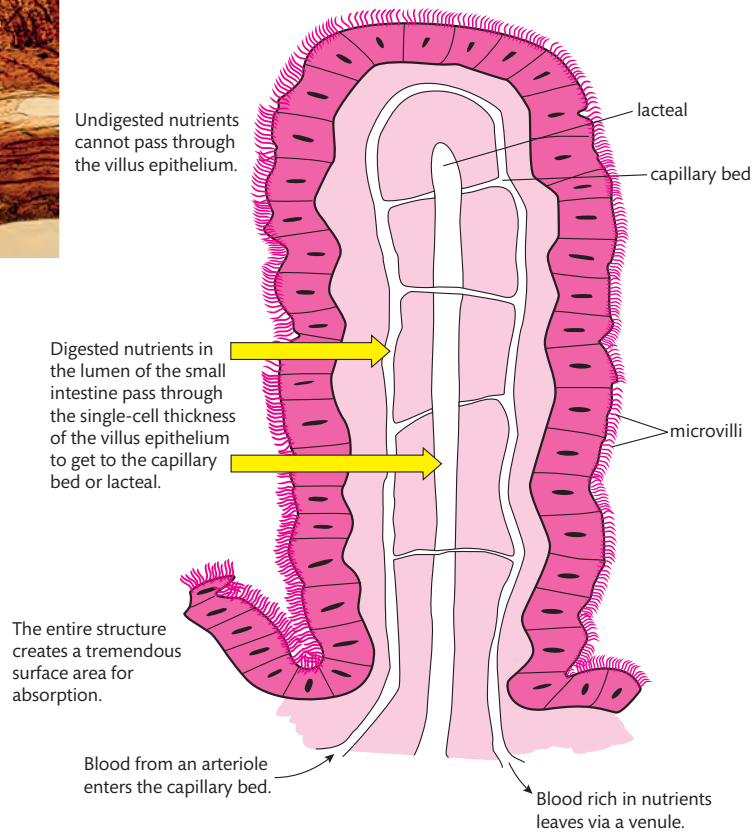


Figure 6.4 The structure of an intestinal villus. It is estimated that each square millimetre of small intestine contains approximately 10–40 villi. Thus the entire small intestine of a human contains millions of villi and even more microvilli.

Transport mechanisms used by epithelial cells to absorb nutrients

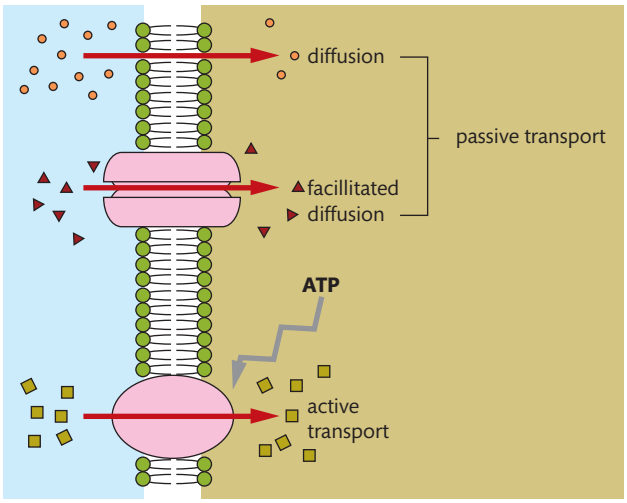


Figure 6.5 Schematic view of three of the more important mechanisms used by cells of the villi epithelium to absorb nutrients from the lumen of the intestine. The mechanism used depends on the size and polarity of the molecule transported. Not shown is endocytosis where a portion of the plasma membrane invaginates to take in many molecules at one time.

A variety of mechanisms are used for nutrient molecules to cross the epithelial layer of the villi mucosa. Here is a summary of some of those transport mechanisms.

Passive mechanisms: no ATP used

- Simple diffusion: direct movement through the cell membrane following a concentration gradient. Examples: very small molecules and non-polar molecules, such as fatty acids, which dissolve through the biphospholipid layer of the membrane.
- Facilitated diffusion: movement through a cell membrane following a concentration gradient, but the molecule must travel through a protein channel because of its size and polarity. Examples: glucose and amino acids.

Active mechanisms: ATP expended

- Membrane pumps: molecules moved against their concentration gradient by certain proteins using ATP to 'pump' the molecule across the membrane. Examples: glucose, and amino acids under certain circumstances.
- Endocytosis (pinocytosis and phagocytosis): molecules are trapped in an invagination (infolding) of the membrane and pass through to the other side of the membrane as a vesicle. Example: some macromolecules that have not yet been fully digested.

Exercises

1. A single sandwich is likely to contain carbohydrates, lipids, and proteins. From a biochemical viewpoint, what happens to each of these types of molecules upon digestion?
2. You ingest a glucose molecule within the starch of a breakfast cereal. List as many locations as you can that this single glucose molecule will visit from the time that it is in your mouth to the time it enters a muscle cell of your body.
3. What role does the pancreas play in the digestive process?

NATURE OF SCIENCE

Theories are regarded as uncertain: William Harvey overturned theories developed by the ancient Greek philosopher Galen on movement of blood in the body.

6.2 The blood system

Understandings:

- Arteries convey blood at high pressure from the ventricles to the tissues of the body.
- Arteries have muscle cells and elastic fibres in their walls.
- The muscle and elastic fibres assist in maintaining blood pressure between pump cycles.
- Blood flows through tissues in capillaries. Capillaries have permeable walls that allow exchange of materials between cells in the tissue and the blood in the capillary.
- Veins collect blood at low pressure from the tissues of the body and return it to the atria of the heart.
- Valves in veins and the heart ensure circulation of blood by preventing backflow.
- There is a separate circulation for the lungs.
- The heart beat is initiated by a group of specialized muscle cells in the right atrium called the sinoatrial node.
- The sinoatrial node acts as a pacemaker.
- The sinoatrial node sends out an electrical signal that stimulates contraction as it is propagated through the walls of the atria and then the walls of the ventricles.
- The heart rate can be increased or decreased by impulses brought to the heart through two nerves from the medulla of the brain.
- Epinephrine increases the heart rate to prepare for vigorous physical activity.

Applications and skills:

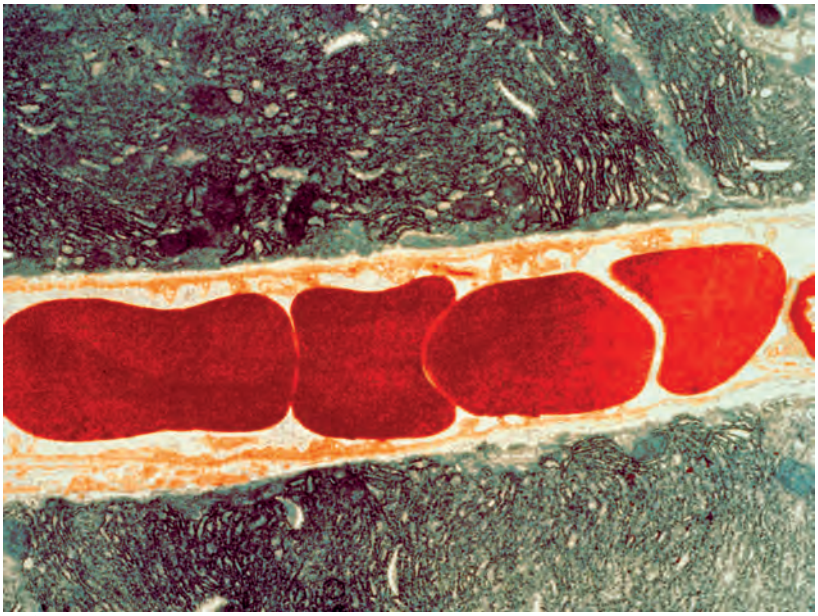
- Application: William Harvey's discovery of the circulation of the blood with the heart acting as the pump.
- Application: Pressure changes in the left atrium, left ventricle, and aorta during the cardiac cycle.
- Application: Causes and consequences of occlusion of the coronary arteries.
- Skill: Identification of blood vessels as arteries, capillaries, or veins from the structure of their walls.
- Skill: Recognition of the chambers and valves of the heart and the blood vessels connected to it in dissected hearts or in diagrams of heart structure.

Arteries, capillaries, and veins

Arteries are blood vessels taking blood away from the heart that has not yet reached a capillary. Veins are blood vessels that collect blood from capillaries and return it to the heart. Identifying a blood vessel as being an artery or a vein has nothing to do with whether the blood is oxygenated or deoxygenated. For example, blood leaving the right ventricle is flowing through pulmonary arteries, even though it needs to be re-oxygenated in the capillaries of the lung tissue. These blood vessels are pulmonary arteries because they are between the heart and the capillary bed. The newly oxygenated blood will be brought back to the heart by the pulmonary veins.

Arteries have a relatively thick, smooth, muscle layer that is used by the autonomic nervous system to change the inside diameter (lumen) of the blood vessels. In addition to smooth muscle, arteries have elastic fibres that help maintain the relatively high blood pressure achieved by the contractions of the ventricles. When blood is pumped into an artery, the elastic fibres are stretched and allow the blood vessel to accommodate the increased pressure. When the contraction is over, the elastic fibres provide another source of pressure as they return to their original position. This helps maintain the blood pressure between pump cycles. Remember that blood in arteries is at a high pressure because arteries are the vessels that are directly connected to the ventricles of the heart. When blood leaves an arteriole (the smallest of the arteries),

it enters a capillary bed rather than a single capillary. A capillary bed is a network of capillaries that typically all drain into a single venule.

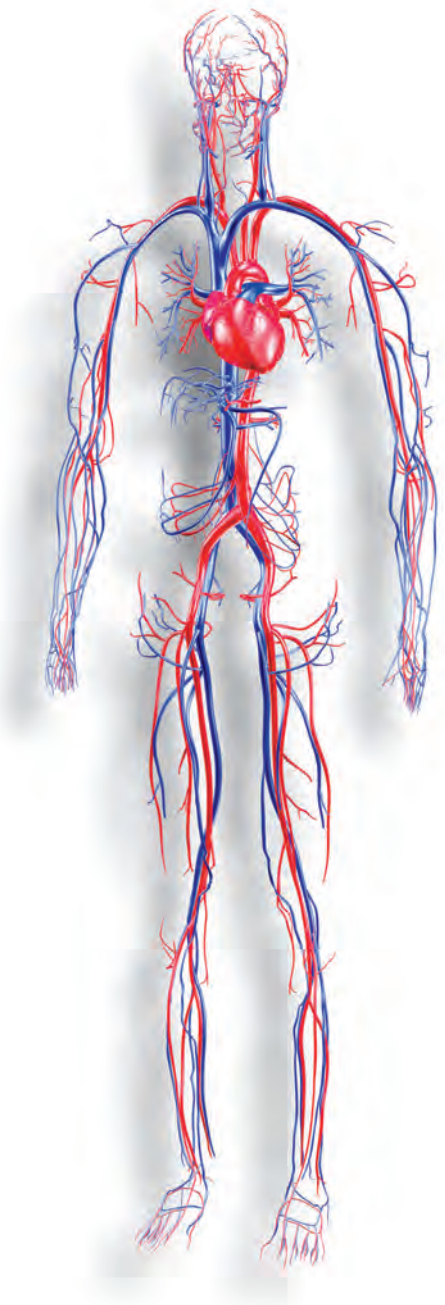


A false-colour transmission electron micrograph (TEM) of a capillary containing erythrocytes (red blood cells). Notice the thin 'wall' of the capillary, which is conducive to the movement of molecules in and out of the bloodstream.

When blood enters a capillary bed much of the blood pressure is lost. Blood cells make their way through capillaries one cell at a time. Chemical exchanges always occur through the single-cell thickness of capillaries, because the walls of arteries and veins are too thick to allow molecules in or out efficiently. Veins receive blood at a relatively low pressure from the capillary beds. Because this blood has lost a great deal of blood pressure, the blood flow through veins is slower than through arteries. To account for this, veins have thin walls and a larger internal diameter. Veins also have many internal passive 'one-way flow' valves that help keep the slow-moving blood travelling consistently towards the heart. Table 6.3 summarizes the three types of blood vessels.

Table 6.3 A comparison of arteries, capillaries, and veins

Artery	Capillary	Vein
Thick walled	Wall is 1 cell thick	Thin walled
No exchanges	All exchanges occur	No exchanges
No internal valves	No internal valves	Internal valves present
Internal pressure high	Internal pressure low	Internal pressure low

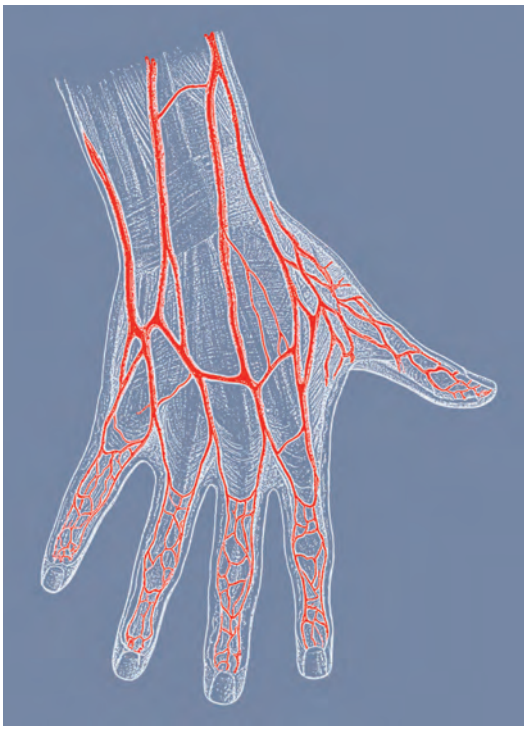


If all the tissue except blood vessels and heart were removed from a body, the shape of the body would still be visible.

Fish have a two-chambered heart and amphibians have a three-chambered heart. Reptiles, birds, and mammals all have a four-chambered heart (although the ventricles of a reptile heart are only partially divided).

The heart, a double pump

The human heart is designed as a pair of side-by-side pumps. Each side of the heart has a collection chamber for the blood that moves in slowly from



A drawing showing some of the larger blood vessels in the hand. Smaller vessels like capillaries cannot be seen without magnification.

the veins. These thin-walled, muscular chambers are called atria. Each side also has a thick-walled muscular pump called a ventricle, which builds up enough pressure to send the blood out from the heart with a force we refer to as blood pressure. This double-sided pump works every minute of every day of your life. The blood that is pumped out from the heart typically makes a circuit through the following sequence of blood vessels:

- a large artery
- smaller artery branches
- an arteriole (the smallest type of artery)
- a capillary bed
- a venule (the smallest type of vein)
- larger veins
- a large vein, which takes the blood back to the heart to be pumped out once again.

The two sides of the heart form two major routes for blood to flow along (see Figure 6.6). The right side of the heart sends blood along a route that is called your pulmonary circulation. Along this route, the capillary beds are found in your lungs, where the blood picks up oxygen and releases carbon dioxide.

The left side of the heart sends blood along a route that is called the systemic circulation. The artery that emerges from the heart at the beginning of this route is the aorta. Branches of the aorta carry blood to almost every organ and cell type in your body. Along this route, the capillary beds are found in your organs and tissues, where the blood picks up carbon dioxide and releases oxygen.

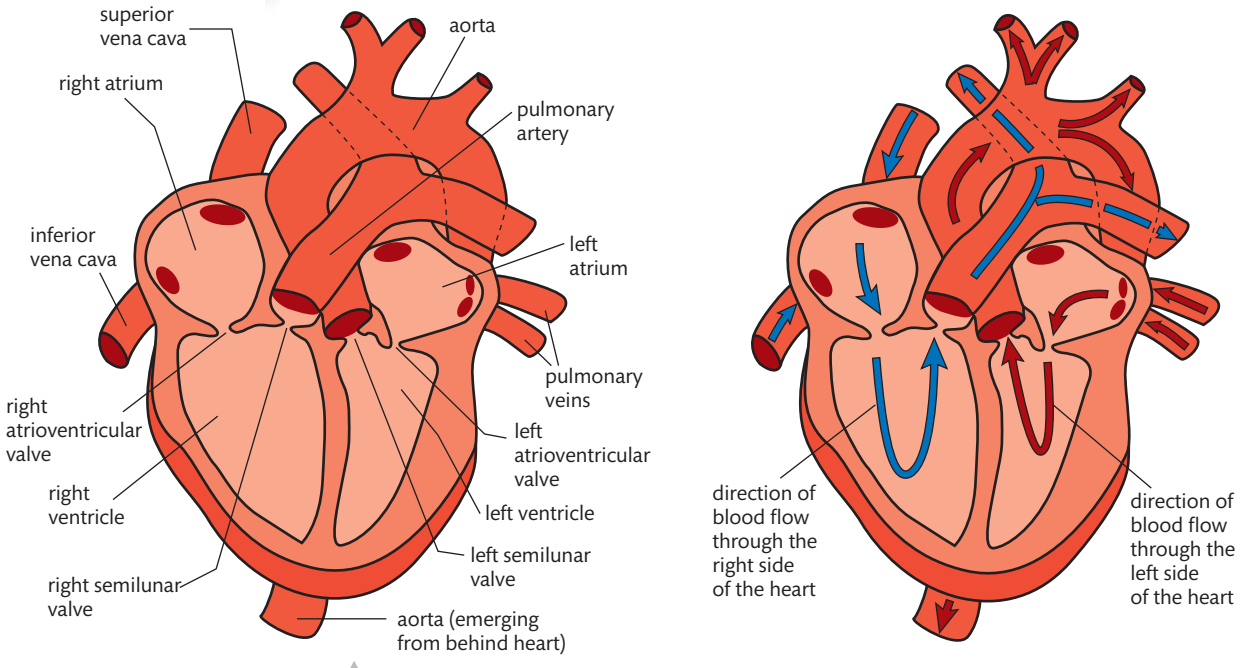


Figure 6.6 Human heart anatomy and blood flow. In the bottom right diagram the blue arrows represent deoxygenated blood and the red arrows represent oxygenated blood.

Control of the heart rate

The majority of the tissue that makes up the heart is muscle. More specifically, it is cardiac muscle. Cardiac muscle spontaneously contracts and relaxes without any control by the nervous system. This is known as myogenic muscle contraction. However, the myogenic activity of the heart does need to be controlled, in order to make the timing of the contractions unified and useful.

Within the right atrium there is a mass of specialized tissue that has properties of both muscle and nervous system cells within its walls; this tissue is called the sinoatrial node (SA node). The SA node acts as the pacemaker for the heart by sending out an 'electrical' signal to initiate the contraction of both atria. For a person with a resting heart rate of 72 beats a minute, the signal from the SA node is sent out every 0.8 seconds. Also within the right atrium is another mass of specialized muscle tissue, known as the atrioventricular node (AV node). The AV node receives the signal from the SA node, delays for approximately 0.1 seconds, and then sends out another 'electrical' signal. This second signal goes to the thick muscular ventricles and results in their contraction. This explains why both atria, and then later both ventricles, contract in synchrony (see Figure 6.7).

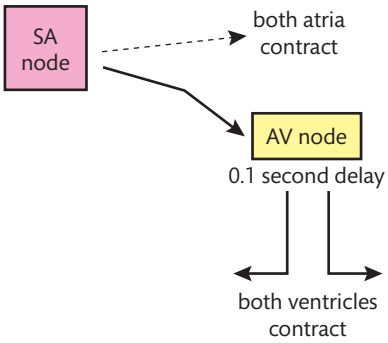
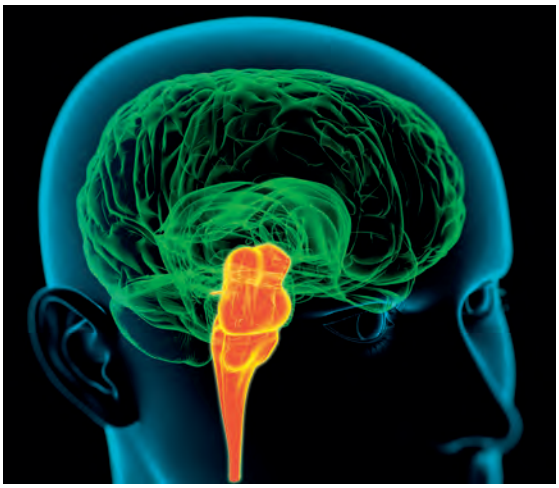


Figure 6.7 Myogenic control of the heart rate. The SA node acts as the pacemaker. The AV node relies on a signal from the SA node to send impulses to the ventricles. Notice the delay between the two events that allows the atria to contract, followed shortly after by the contraction of the ventricles.

During times of increased body activity, such as exercise, the heart rate needs to increase above the resting heart rate. This is because there is an increased demand for oxygen for cell respiration during periods of heavy exercise or activity. There is also a need to get rid of the increased levels of carbon dioxide that accumulate in the bloodstream. As exercise begins and carbon dioxide levels begin to rise, an area of your brainstem called the medulla chemically 'senses' the increase in carbon dioxide.



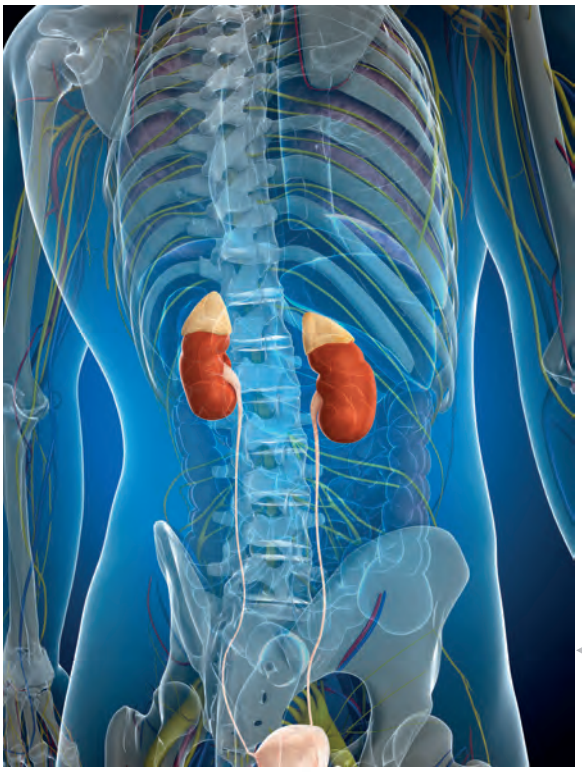
Much of the orange area of this computer artwork shows an area of the brainstem called the medulla (oblongata). Chemoreceptors in the medulla are sensitive to carbon dioxide changes in the blood as it passes through.

CHALLENGE YOURSELF

1 Study the left part of Figure 6.6 and learn the names of the chambers, valves, and blood vessels associated with the heart. Then cover up the diagram and follow an imaginary red blood cell through the complete circulation pattern as shown in the right part of the figure. When you can do this without any mistakes, cover the right diagram and use the left diagram to trace the blood flow, noting at each location whether the blood is oxygenated or deoxygenated.

The increase in number of chambers of the heart, from the two characteristic of fish to the four characteristic of birds and mammals, allows complete separation of deoxygenated and oxygenated blood. In other words, the evolution of the four-chambered heart led to the separation of the pulmonary and systemic circulations.

As you continue your study of human physiology, look for instances where two or more systems of the body interact in order to accomplish an action. For example, during exercise, your heart rate cannot increase or return to its resting heart rate without the nervous system and the circulatory system interacting.



Computer artwork showing the two kidneys in a male. The lighter coloured tissue on the upper portion of each kidney is an adrenal gland. Like all endocrine glands, adrenal glands secrete their hormone (epinephrine) into the bloodstream for distribution to all parts of the body.

The medulla then sends a signal through a cranial nerve, called the cardiac nerve, to increase the heart rate to an appropriate level. This signal is sent to the SA node; it does not change the mechanism of how the heart beats, just the timing. After exercise, the level of carbon dioxide in the bloodstream begins to decrease and another signal is sent from the medulla. This time the signal is carried by a different cranial nerve, called the vagus nerve. Electrical signals from the vagus nerve result in the SA node once again adjusting the timing of the heart rate, so that the heart returns to its myogenic or resting heart rate.

The heart rate can also be influenced by chemicals. One of the most common is epinephrine (also called adrenaline). During periods of high stress or excitement, your adrenal glands secrete epinephrine into the bloodstream. Among other effects, epinephrine causes the SA node to 'fire' more frequently than it does at its resting heart rate, and thus the heart rate increases, sometimes dramatically so.

CHALLENGE YOURSELF

2 Try to verbalize the events that lead to the following.

- The contraction of both atria followed by contraction of both ventricles for a person who is currently at his or her resting heart rate.
- The increase in heart rate for a person who has recently begun exercising.
- The decrease in heart rate for a person who has recently stopped exercising.

A (single) cardiac cycle is what most people think of as a 'heart beat'. A cardiac cycle is initiated by the SA node impulse and includes all the heart events that follow until another SA node signal begins a new cardiac cycle.

Changes in pressure within the heart chambers keep the blood moving

Heart valves open and close depending on the pressure of the blood on each side of the valve. The change in pressure also explains the movement of blood through and out of each chamber of the heart. Both the left and right sides of the heart work synchronously as a double pump. To understand the workings of the heart, it is only necessary to look at one side of the heart with the understanding that the other side has similar pressures and volumes of blood at the same time.

Let's examine the pressure and volume changes that occur on the left side of the heart. You do not have to memorize the pressure numbers given in this example, your focus should be on understanding how the given blood pressures result in the movement of blood and the opening and closing of the heart valves.

When both chambers are at rest

The term used for a chamber of the heart that is not contracting is diastole. The term used for a chamber of the heart that is contracting is systole. Thus the time period when both chambers are at rest can be described as both chambers undergoing diastole.

Figure 6.8 shows the left side of the heart with openings in the left atrium for entry of the pulmonary veins. The numbers inside each chamber or blood vessel represent the pressure measured in mm Hg. Heart valves open and close based on blood pressure differences on either side of any one valve. During this period of diastole for both chambers, the atrial pressure is just slightly higher than ventricular pressure, and

this keeps the left atrioventricular valve open. Much of the blood that slowly returns to the left atrium via the pulmonary veins moves passively down to the left ventricle through this open valve. Notice also that the pressure in the aorta is much higher than in the left ventricle. This pressure difference keeps the left semilunar valve closed and prevents backflow into the ventricle.

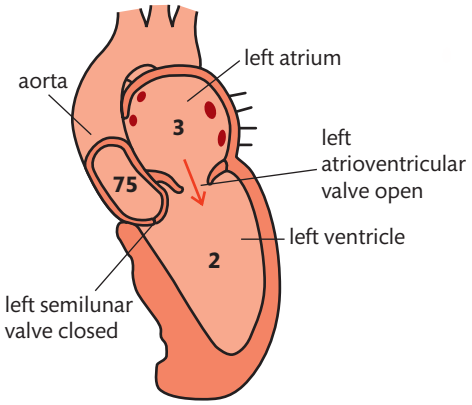
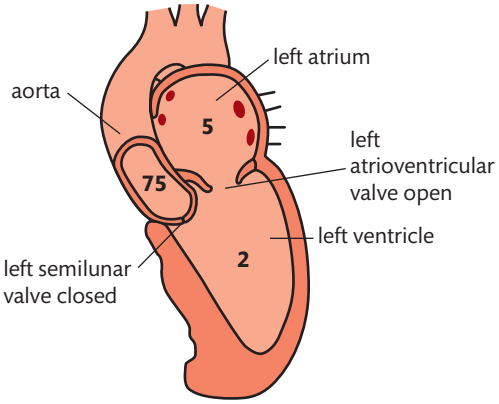


Figure 6.8 Blood pressure readings in mm Hg when both chambers are in diastole (rest). Notice that some blood is moving passively from the left atrium to the left ventricle.

When the atria are in systole and the ventricles are in diastole

In Figure 6.9, the atrium is undergoing a systole (contraction). The pressure produced by this systole is not very high. The wall of each atrium is relatively thin muscle and is not capable of creating very much pressure. There is no need for great pressure because much of the volume of blood has already accumulated passively within the ventricle through the open atrioventricular valve. Any remaining blood in the atrium is moved to the ventricle by the systole.



The muscular walls of both atria are very thin, and the pressure exerted during atrial systole is very low. Conversely, the muscular walls of the ventricles are very thick, and the pressure exerted during ventricular systole is very high.

Figure 6.9 Typical blood pressure readings in mm Hg during atrial systole.

When the atria are in diastole and the ventricles are in systole

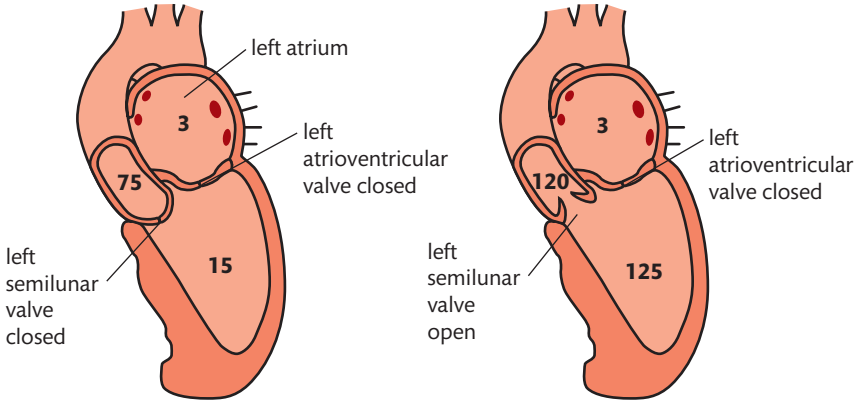


Figure 6.10 Blood pressure readings in mm Hg at early and late ventricular systole.

Figure 6.10 shows the blood pressures in early and late ventricular systole. As soon as ventricular systole begins, the pressure inside the ventricle increases to be greater than that in the atrium, so the atrioventricular valve closes to prevent backflow to the atrium (this creates the 'lub' sound that can be heard with a stethoscope). The pressure in the aorta is still far higher than in the ventricle, so the semilunar valve

Blood pressure is often measured in mm Hg, although the modern units for pressure are pascals (Pa) and kilopascals (kPa).

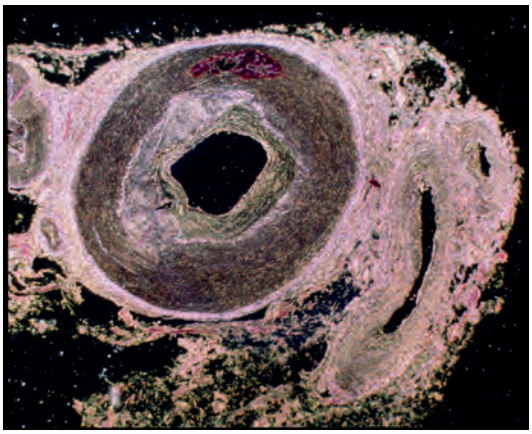
120 mm Hg = 16 kPa

80 mm Hg = 11 kPa

The mean population blood pressure varies widely from country to country. As a general rule, high blood pressure is positively correlated with the consumption of salt and obesity, and is negatively correlated with the consumption of fruits and vegetables.

remains closed. There is a relatively large volume of blood in the ventricle during this time, and the ventricle is highly muscular. This combination of factors permits the ventricular pressure to build up considerably as systole continues. Finally, the pressure in the ventricle becomes greater than that in the aorta, and the semilunar valve opens, allowing the ventricle to pump the blood into the aorta. As the ventricle finishes its contraction, the pressure inside it once again drops below the pressure in the aorta, and the semilunar valve closes (this causes the 'dub' sound that can be heard with a stethoscope). Both chambers go back into diastole and the cardiac cycle repeats itself again, and again.

Build-up of plaque in arteries leads to atherosclerosis



An artery showing artherosclerosis. The dark area in the centre is the lumen, where blood flows. The light grey area surrounding the lumen is plaque. The lumen of this blood vessel is significantly smaller than it was at an earlier time in this person's life.

Atherosclerosis is a slow build-up of materials in the arteries that is collectively called plaque. Plaque is composed of lipids, cholesterol, cell debris, and calcium. The build-up of this material begins early in life and typically takes many, many years to become a serious problem. As arteries begin to build up plaque, they become harder and therefore less flexible. The inside lining of an artery is known as the endothelium. In a young person, the endothelium of each artery is smooth, with no plaque build-up. As the years progress, each person begins to deposit plaque. How much depends on a whole set of factors, with genetics and eating habits being of prime importance.

Occlusion in coronary arteries can lead to a heart attack

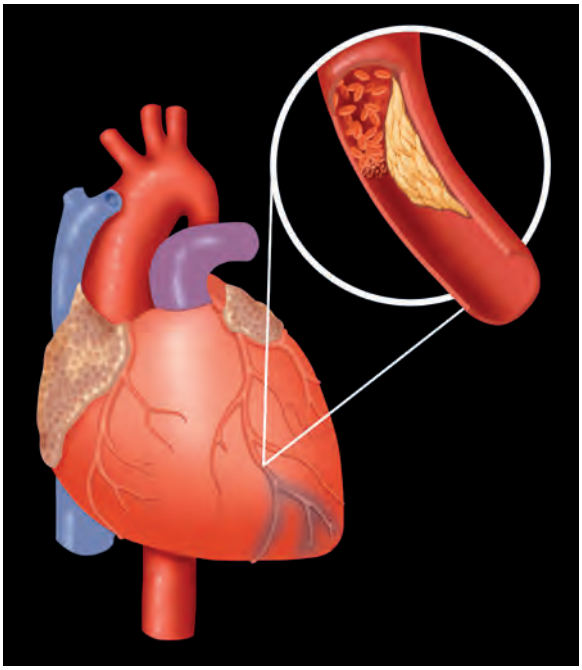


Illustration showing an occlusion (a clot caused by plaque build-up) in a coronary artery.

The heart has three major coronary arteries that supply the heart muscle with oxygen-rich blood. These arteries are branches direct from the aorta and carry blood that has recently been to the lungs. As you will recall, cardiac muscle never stops contracting, with alternating periods of systole and diastole occurring repeatedly throughout your life. Thus cardiac muscle is very oxygen-demanding. If any one of the three major coronary arteries, or one or more of their branches, is somehow blocked, some portion of the heart muscle is likely to be deprived of its oxygen supply. This is exactly what happens when atherosclerosis eventually leads to a partial or complete occlusion. The term occlusion describes the condition when plaque build-up has become so substantial that the blood vessel can no longer supply even a minimally healthy volume of blood to the tissue that it 'feeds'.

When a coronary artery or one of its main branches becomes blocked, it is known as a coronary thrombosis or an acute myocardial infarction, i.e. a heart attack.

NATURE OF SCIENCE

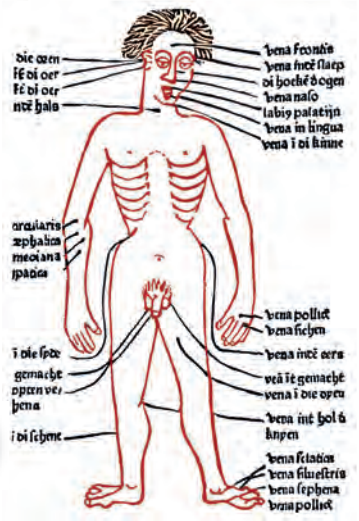
Have you ever thought about how difficult it would be to convince everyone around you that something they and everyone else had been taught and firmly believed in was actually false? Especially something that has been believed for many centuries?

It would be an exceptionally difficult thing to do, and attempting to do this might mean you are considered to be a lunatic.

A man by the name of William Harvey made such an attempt after his experimental work showed how blood is circulated around the body. Prior to Harvey's experimental work, the authority on the movement of blood in the body was provided by the early Greeks (AD 100–200), including Pliny the Elder and Galen (of Pergamon). These Greeks postulated that blood was constantly being used up within the body, and they did not consider the closed circulation pattern we now know exists. Galen taught his students that there were two types of blood: 'nutritive blood' that was made by the liver, and 'vital blood' that was made by the heart and distributed through the arteries to carry the 'vital spirits'. Further, Galen taught his students that blood flowed from one ventricle of the heart to the other through tiny pores. In order to understand the context of Galen's teachings, you must imagine blood that is not flowing through blood vessels as we think of now, but rather seeping slowly from one location to another until the blood in the body is 'used up'. The latter was the thinking of virtually every person trained in medicine for more than 1300 years.

After years of animal dissections, live animal experimentation, and human cadaver dissections, William Harvey determined that the heart acts as a double pump (with systemic and pulmonary circulations), and that the blood is continuously circulated to/from the lungs and to/from the body. He was not able to see the capillaries that connected arteries to veins, but he postulated their existence. In 1628, Harvey published his work in a publication called *On the Movement of the Heart and Blood in Animals*. As you might imagine, at first many people did not believe Harvey's teachings. The nature of science sometimes dictates that good, new scientific knowledge takes time to become trusted.

A leech, sometimes used for bloodletting procedures. A leech can increase its body size considerably after feeding on a blood meal.



15th-century illustration of common bloodletting sites. The labelling is the original Latin. Bloodletting was sometimes done by making cuts and sometimes by the application of leeches.

Bloodletting was a common medical procedure that was based on Galen's theory of circulation. Bloodletting was a procedure whereby small cuts were made in order to drain blood from certain areas of the body. The thinking was that blood and other bodily 'humours' (fluids) needed to be in balance, and an illness was often attributed to these humours being out of balance. Bloodletting was believed to restore the healthy balance.

Exercises

4 Identify all the heart chambers, valves, and blood vessels involved in one complete circuit of blood (only blood vessels immediately entering or exiting the heart need to be named). Name these in the order the blood passes through them, starting with the right atrium.

5 Before birth, a human foetus has a hole between the right atrium and left atrium. Work out how that changes the blood flow within the foetal circulation, and why foetal circulation has evolved such a pattern.

6 What causes heart valves to open and close?

NATURE OF SCIENCE

Risks associated with scientific research: Florey and Chain's tests on the safety of penicillin would not be compliant with current protocol on testing.

The world that we live in is literally infested with viruses and bacteria. Only a very, very small percentage of these are pathogenic to human beings; in fact, the vast majority of bacteria are very useful.

6.3 Defence against infectious disease

Understandings

- The skin and mucous membranes form a primary defence against pathogens that cause infectious disease.
- Cuts in the skin are sealed by blood clotting.
- Clotting factors are released from platelets.
- The cascade results in the rapid conversion of fibrinogen to fibrin by thrombin.
- Ingestion of pathogens by phagocytic white blood cells gives non-specific immunity to diseases.
- Production of antibodies by lymphocytes in response to particular antigens gives specific immunity.
- Antibiotics block processes that occur in prokaryotic cells but not in eukaryotic cells.
- Viruses lack a metabolism and cannot therefore be treated with antibiotics. Some strains of bacteria have evolved with genes that confer resistance to antibiotics, and some strains of bacteria have multiple resistance.

Applications and skills

- Application: Causes and consequences of blood clot formation in coronary arteries.
- Application: Florey and Chain's experiments to test penicillin on bacterial infections in mice.
- Application: Effects of HIV on the immune system and methods of transmission.

Guidance

- *Diagrams of skin are not required.*
- *Subgroups of phagocyte and lymphocyte are not required but students should be aware that some lymphocytes act as memory cells and can quickly reproduce to form a clone of plasma cells if a pathogen carrying a specific antigen is re-encountered.*
- *The effects of HIV on the immune system should be limited to a reduction in the number of active lymphocytes and a loss of the ability to produce antibodies, leading to the development of AIDS.*

Primary defence is to keep pathogens out

Our bodies are exposed to many disease-causing agents. Any living organism or virus that is capable of causing a disease is called a pathogen. Pathogens include viruses, bacteria, protozoa, fungi, and worms of various types. Yet exposure to the vast majority of pathogens does not result in a disease. Primarily, this is because we are too well defended for most pathogens to enter our bodies and, if any do manage to enter, we have often previously developed immunity to that pathogen. For some pathogens, such as bacteria, there are chemicals called antibiotics that can work against the living bacterial cells but do not affect our body cells. Let's explore more about this interesting and important topic.

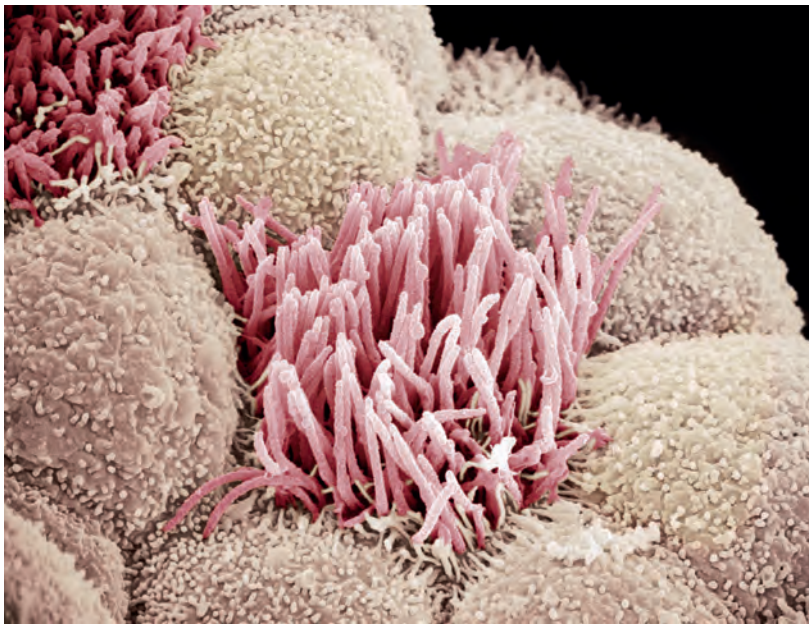
Skin and mucous membranes form a primary defence

The best way to stay healthy is to prevent pathogens from having the chance to cause disease. One way to do this is to try to stay away from sources of infection. This is why it is still common to isolate (or quarantine) people who have highly transmittable diseases. Obviously, it is not possible to isolate yourself from every possible source of infection. Therefore, the human body has some ingenious ways of making it difficult for pathogens to enter it and start an infection.

One of those ingenious ways is your skin. Think of your skin as having two primary layers. The underneath layer is called the dermis and is very much alive. It contains sweat glands, capillaries, sensory receptors, and dermal cells, which give structure and

strength to the skin. The layer on top of this is called the epidermis. This epidermal layer is constantly being replaced as the underlying dermal cells die and are moved upwards. This layer of mainly dead cells forms a good barrier against most pathogens because it is not truly alive. As long as our skin remains intact, we are protected from most pathogens that can enter living tissues. This is why it is important to clean and cover cuts and abrasions of the skin when they do occur.

Pathogens can enter the body at a few points that are not covered by skin. These entry points are lined with tissue cells that form a mucous membrane. Cells of mucous membranes produce and secrete a lining of sticky mucus. This mucus can trap incoming pathogens and so prevent them from reaching cells that they could infect. Some mucous membrane tissue is lined with cilia. Cilia are hair-like extensions capable of a wave-like movement. This movement moves trapped pathogens up and out of mucous-lined tissues such as your trachea. Table 6.4 shows some common areas that have a mucous membrane.



False-colour scanning electron micrograph (SEM) of the mucous membrane lining of the trachea. The large white cells are called goblet cells and they secrete mucus. Hair-like cilia (in pink) are also visible.

Table 6.4 The locations of mucous membranes

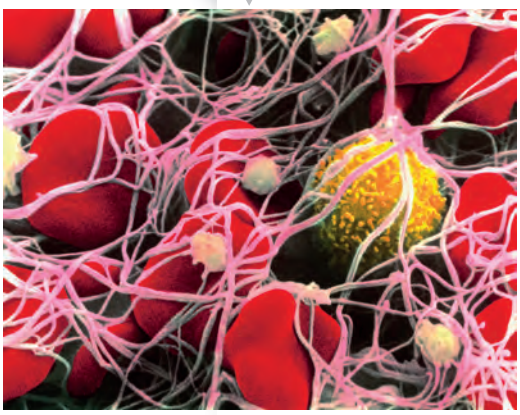
Area with a mucous membrane	What it is and does
Trachea	The tube that carries air to and from the lungs
Nasal passages	Tubes that allow air to enter the nose and then the trachea
Urethra	A tube that carries urine from the bladder to the outside
Vagina	The reproductive tract leading from the uterus to the outside

According to an article published by the National Institute of Health (NIH), bacteria outnumber their human hosts by about 10 to 1 cells. In a typical human adult, bacteria would account for about 2% of his or her body mass.

Blood clotting minimizes the chances of infection and blood loss

When small blood vessels like capillaries, arterioles, and venules are broken, blood escapes from the closed circulatory system. Often the damaged blood vessels are in the skin, and so pathogens then have a way to gain entry into the body. Our bodies have evolved a set of responses to create a clot that 'seals' the damaged blood vessels, so preventing excessive blood loss and helping prevent pathogens from entering the body.

Circulating in the blood plasma are a variety of molecules called plasma proteins. These proteins serve many purposes, including



This false-colour SEM shows that small platelets (shown in pale green) have triggered the formation of insoluble fibrin protein fibres. Trapped in the fibrin are several red blood cells, platelets, and one white blood cell (shown in yellow).

some that are involved in clotting. Two of the clotting proteins are prothrombin and fibrinogen. These two molecules are always present in blood plasma, but remain inactive until 'called to action' by events associated with bleeding. Also circulating in the bloodstream are cell fragments known as platelets. Platelets form in the bone marrow, along with red blood cells (erythrocytes) and white blood cells (leucocytes), but do not remain as entire cells. Instead, one very large cell breaks down into many fragments, and each of the fragments becomes a platelet. Platelets do not have a nucleus and they have a relatively short cellular life span, of about 8–10 days.

Let's consider what happens when a small blood vessel is damaged (see Figure 6.11). The damaged cells of the blood vessel release chemicals that stimulate platelets to adhere to the damaged area. The damaged tissue and platelets release chemicals called clotting factors that convert prothrombin into thrombin. Thrombin is an active enzyme that catalyses the conversion of soluble fibrinogen into the relatively insoluble fibrin. The appropriately named fibrin is a fibrous protein that forms a mesh-like network that helps to stabilize the platelet plug. More and more cellular debris becomes trapped in the fibrin mesh, and soon a stable clot has formed, preventing both further blood loss and the entry of pathogens.

Haemophilia is an inherited blood-clotting disorder. Haemophiliacs lack the ability to produce one of the chemicals needed for normal clotting.

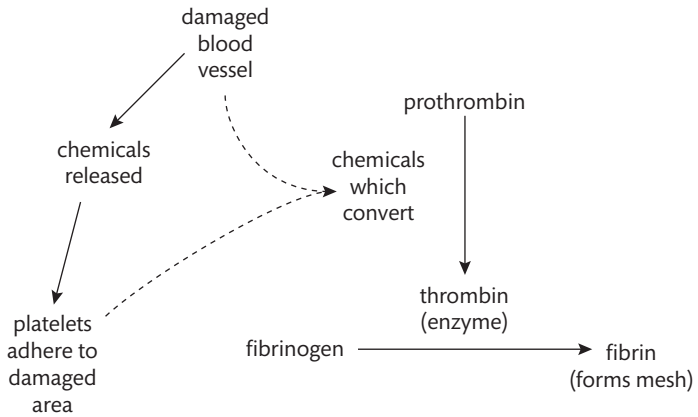


Figure 6.11 Flowchart of the blood-clotting sequence. The sequence starts with a damaged blood vessel, and leads to a meshwork of fibrin that traps blood cells to form a clot. The image on page 285 shows blood cells trapped in fibres of fibrin.

When pathogens get past skin and mucous membranes

Travel between far-reaching areas of our world has increased tremendously in the last century. With that increase in travel has come an associated increase in the rate of spread of global disease.

When a pathogen, such as a pathogenic bacterial species, does enter the body, a series of events begins known as the immune response. If this is a first encounter with a particular pathogen, the response is known as a primary immune response. If it is a second (or third, etc.) encounter, the response is known as a secondary immune response. A primary immune response takes at least a week or more to be successful, and thus it is common to experience the symptoms associated with a disease while the immune system is working to reduce and finally eliminate the pathogen. A secondary immune response is both quicker and more intense, and thus symptoms are rarely experienced. The ability to accomplish a secondary immune response for a particular antigen is actually what we call being 'immune' to a disease.

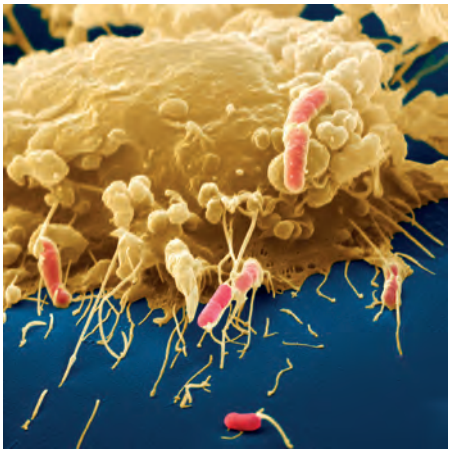
Role of phagocytic white blood cells

White blood cells (leucocytes) are the cells in our bloodstream that help us fight off pathogens that enter our bodies, and also provide us with immunity for the many pathogens that we encounter more than once. One type of leucocyte that is involved

very early on in the process of fighting off a pathogen is called a macrophage. Macrophages are large leucocytes that are able to change their cellular shape to surround an invading cell through the process of phagocytosis. Because macrophages can easily change their shape, they are able to squeeze their way in and out of small blood vessels. Therefore, it is not unusual for a macrophage to first encounter an invading cell outside the bloodstream.

When a macrophage meets a cell, it can recognize whether that cell is a natural part of the body and therefore 'self', or not part of the body and therefore 'not-self'. This recognition is based on the protein molecules that make up part of the surface of all cells and viruses. If the collection of proteins the macrophage encounters on a cell is determined to be 'self', then the cell is left alone. If the determination is 'not-self', the macrophage engulfs the cell by phagocytosis. Phagocytes typically contain many lysosome organelles, in order to digest chemically whatever has been engulfed. This type of response by the body is called non-specific, because the identity of the specific pathogen has not been determined, just the fact that it is something that is 'not-self' and therefore should be removed.

The role of macrophages in determining self versus not-self cells is called non-specific immunity, even though no real immunity is gained by the action of the macrophages.

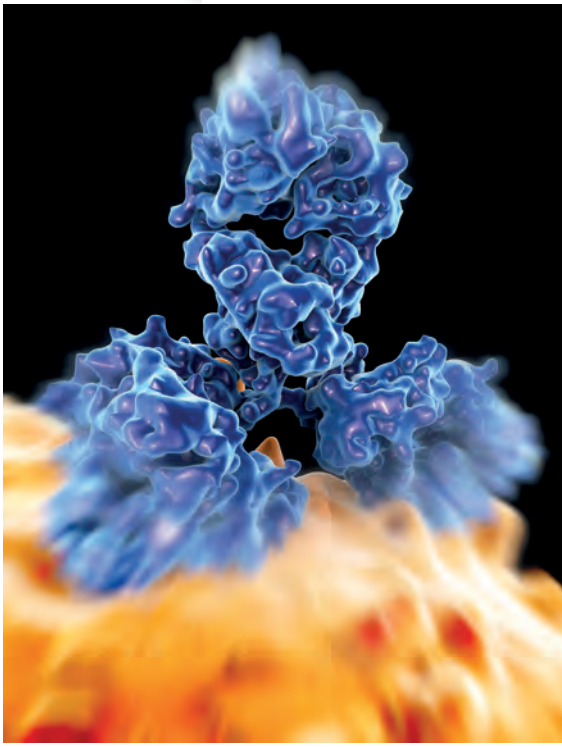


False-colour SEM showing a macrophage (the large yellow cell) engulfing *Escherichia coli* bacteria (the small pink rods).

Antibodies produced by lymphocytes lead to specific immunity

Antibodies are protein molecules that are produced by the body in response to a specific type of pathogen. In other words, if you had a measles infection, you would produce one type of antibody, and if you contract a virus that gives you influenza (flu), you would produce another type of antibody. Each type of antibody is different because each type has been produced in response to a different pathogen. Each pathogen is made up of either cells with cell membranes or, in the case of a virus, a protein coat called a capsid. The cellular invaders, such as bacteria, have proteins that are embedded in their outer surface. In the language of the immune system, these foreign proteins are called antigens. You have just learned that 'not-self' proteins trigger an immune response. All of these 'not-self' proteins are antigens.

Each antibody is a protein that is Y-shaped. At the end of each of the forks of the Y is a binding site. The binding site is where an antibody attaches itself to an antigen. Because the antigen is a protein on the surface of a pathogen (such as a bacterium), the antibody thus becomes attached to the pathogen (see the artwork on the right).

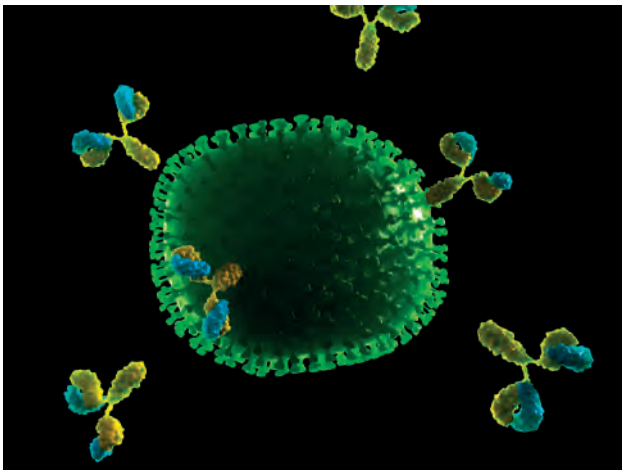


Computer artwork showing an antibody attaching to a cell surface. One way antibodies function is to attach to and thus 'mark' a cell for destruction by certain types of leucocytes.

The leucocytes that produce antibodies are a type of cell called plasma cells. Each of us has many different types of antibody-producing plasma cells and, as a general rule, each type of plasma cell can produce only one type of antibody. The problem is, each cell only produces a relatively small number of antibodies in comparison with the massive infection that may be present in the body. However, our continually evolving immune response has a way of producing many of the same type of plasma cells when they are needed. Here are the steps of a typical primary immune response.

1. A specific antigen type is identified (e.g. a particular cold virus).
2. A specific plasma cell is identified that can produce an antibody that will bind to the antigen (e.g. the proteins of the capsid coat of the cold virus).
3. The specific plasma cell type clones itself (divides repeatedly by mitosis) to increase rapidly the numbers of that type of plasma cell.
4. The newly formed 'army' of specific plasma cells begins antibody production.
5. The newly released antibodies circulate in the bloodstream and eventually find their antigen match (e.g. the proteins of the virus capsid).
6. Using various mechanisms, the antibodies help eliminate the pathogen.
7. Some of the cloned antibody-producing plasma cells remain in the bloodstream and provide immunity against a second infection by the same pathogen. These long-lived cells are called memory cells.
8. Memory plasma cells of this type respond quickly if the same antigen is encountered again (a secondary immune response).

Vaccines are weakened or non-pathogenic forms of pathogens that cause a primary immune response within your body. This leads to the production of the same memory lymphocytes as the actual disease does. Thus, following a vaccination, if you do encounter the actual pathogen, the memory cells will initiate a very quick secondary immune response. In most instances, the secondary immune response is so quick that symptoms associated with the pathogen do not have time to develop.



Artwork showing antibodies binding to a flu virus. Each antibody is uniquely designed to fit an antigen. This is part of your specific immunity, because of the specificity of the molecules involved in the 'match'.

What is HIV and how does it affect the human immune system?

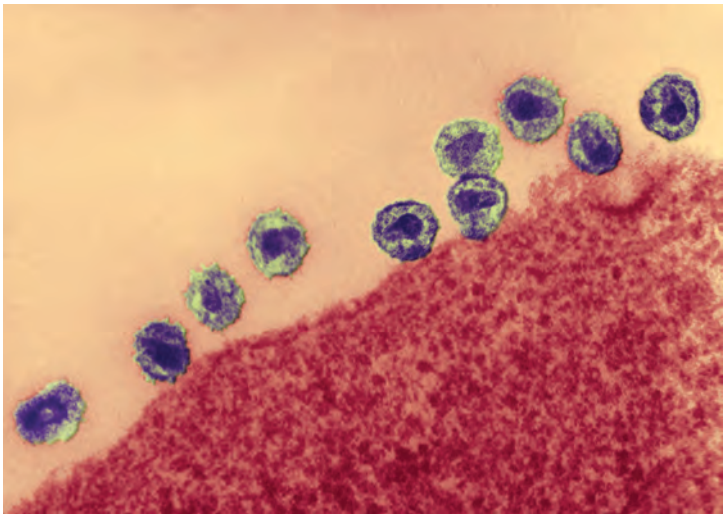
HIV is the abbreviation for a virus called human immunodeficiency virus. Just like any virus, HIV is very specific about which organisms and which cell types in an organism it infects. Unfortunately, the infected (host) cells in humans is one of the

key lymphocyte cell types involved in the immune responses just described. A person infected with HIV will eventually experience a severe drop in his or her lymphocyte population, and will lose the ability to produce adequate antibodies. It typically takes many years after the initial infection by HIV before an infected person loses his or her specific immune response capability, but when it does happen the resulting immune disease is called AIDS or acquired immune deficiency syndrome.

When the symptoms of AIDS do begin, the infected person can no longer fight off pathogens as he or she could before, and a multitude of infections of various types begins. It is one or more of these secondary infections that most often takes the life of someone with AIDS. At the time of publication of this text, no effective treatment has been found to cure someone with an HIV infection. However, a variety of treatments have been found that are prolonging the time period between infection and the onset of symptoms of AIDS.

How is HIV transmitted?

The two most common ways that HIV is spread from person to person is by having unprotected sex with an infected person, and by using a hypodermic needle that has previously been used by someone who is HIV-positive (HIV^+). In addition, it is possible for an HIV^+ mother to infect her child during pregnancy, labour, delivery, or breastfeeding. In some countries, receiving a blood transfusion can spread HIV, but that is no longer a risk in countries where blood and blood products are routinely tested for contamination. Some medical treatments, such as injections for treating haemophilia, have been known to spread HIV when the injection was purified from human blood. In many areas of the world, these products are now produced by genetically engineered bacteria and have no risk of transmitting HIV.



A false-colour TEM of HIV (small round objects) infecting a leucocyte.

TOK

Do scientific researchers have a responsibility to communicate and collaborate freely with each other? Sometimes a competitive environment, striving to be the first to discover something, can get in the way of productive collaboration. An example was the limited collaboration between competing USA and French research teams in the early days of research on the pathogen that we now know as HIV.

The use of antibiotics to combat bacterial infections

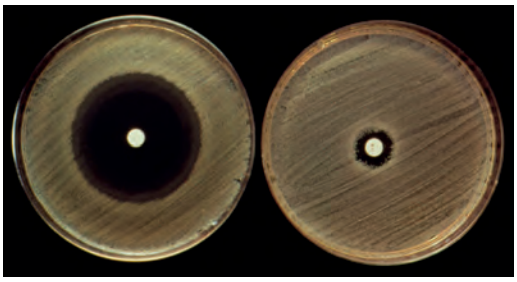
Bacteria are prokaryotic cells. Humans and other animals are composed of eukaryotic cells. There are major structural and biochemical differences between prokaryotic and eukaryotic cells. For example, protein synthesis is similar in both types of cell, but not exactly the same. Also, bacteria have a cell wall, a structure not characteristic of eukaryotic animal cells. Antibiotics are chemicals that take advantage of the differences

between prokaryotic and eukaryotic cells, and selectively block some of the biochemistry needed by bacteria while having no effect on human or animal cells. There are many categories of antibiotics, depending on the biochemical pathway that is being targeted. One type of antibiotic may selectively block protein synthesis in bacteria, but have no effect on our cells' ability to manufacture proteins. Another type may inhibit the production of a new cell wall by bacteria, thus blocking their ability to grow and divide.

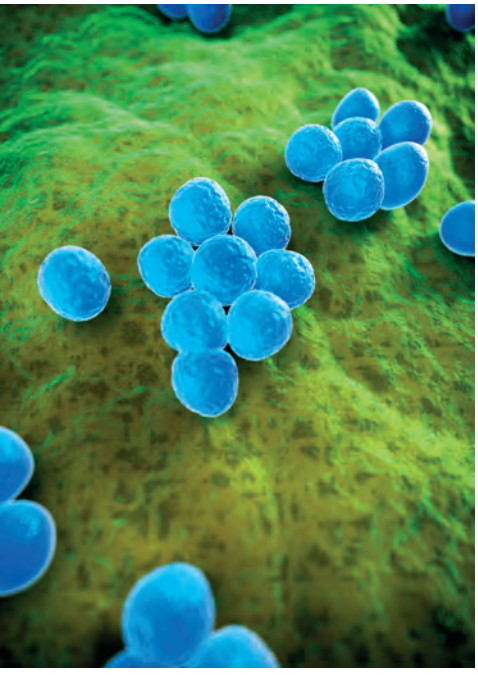
This also explains why antibiotics have no effect on viruses. Viruses make use of our own body cells' metabolism to create new viruses. Any chemical that could inhibit this would also be damaging to our own body cells. Thus antibiotics are chemicals with the ability to damage or kill prokaryotic cells, but not damage eukaryotic cells or their metabolism; because a virus has no metabolism of its own, antibiotics are not prescribed for any disease of viral origin.

NATURE OF SCIENCE

Alexander Fleming made the initial discovery of penicillin in 1928. However, Fleming became frustrated by his inability to isolate the chemical from the fungus that produced the antibiotic, and moved on to other work. About a decade later, Ernst Chain and Howard Florey picked up on Fleming's work and isolated a small amount of the penicillin compound. They injected eight mice with a deadly bacterial species and four of these mice were also injected with the newly isolated penicillin. The four mice that were not injected with penicillin all died within a day. The four mice that were injected with penicillin all lived for several days. Small-scale studies such as this would in fact have little credibility by the standards used today to judge the validity of experimental work.



At the centre of each Petri dish is a tablet of penicillin. As you can see, growth of the strain of bacteria on the left is greatly inhibited by the penicillin that is diffusing outwards from the pellet. The strain of bacteria on the right is a strain that has developed a resistance to penicillin and its growth is not nearly as inhibited.



Computer artwork showing MRSA bacteria (small blue spheres).

An unsolved dilemma: bacterial resistance to antibiotics

Remember that any one antibiotic is a specific chemical that selectively targets some aspect of prokaryotic cell biochemistry that is different from eukaryotes. Bacteria show genetic variation just like all other living organisms on Earth. Because bacterial population numbers can be incredibly large, and because bacteria can reproduce very quickly, the mathematical odds that within a bacterial population a genetic variant exists that is not affected by any one antibiotic is quite possible. That one (or a few) variant can then reproduce and repopulate a colony in a very short period of time with bacteria that are all resistant to the antibiotic. The surviving resistant bacteria would then be a new strain of bacteria.

The long-term use and overuse of antibiotics has now led to many pathogenic species of bacteria that have strains that are resistant to nearly all of the antibiotics in existence today.

Some strains of bacteria are even resistant to multiple antibiotics. *Staphylococcus aureus* is a bacterium that can be pathogenic, resulting in what many call a 'staph infection'. Some strains of *S. aureus* are referred to as MRSA (pronounced 'mersa'): these are strains of *S. aureus* that have developed a resistance to many types of antibiotics. MRSA infections are very difficult to treat and are becoming more and more frequent.

Exercises

7 Why are some pathogenic viruses potentially lethal (e.g. HIV, *Ebola*), while others result in only fairly mild and temporary symptoms?

8 Distinguish between non-specific and specific immune responses.

9 What is a virus doing when it is not infecting a host cell?

10 In the very early years of research on the disease that we now know as AIDS, government funding for research was close to non-existent. Other than the fact that it was a fairly 'new' disease, can you think of one or more reasons why funding was so low?

6.4 Gas exchange

NATURE OF SCIENCE

Obtain evidence for theories: epidemiological studies have contributed to our understanding of the causes of lung cancer.

Understandings:

- Ventilation maintains concentration gradients of oxygen and carbon dioxide between air in alveoli and blood flowing in adjacent capillaries.
- Type I pneumocytes are extremely thin alveolar cells that are adapted to carry out gas exchange.
- Type II pneumocytes secrete a solution containing surfactant that creates a moist surface inside the alveoli to prevent the sides of the alveolus adhering to each other by reducing surface tension.
- Air is carried to the lungs in the trachea and bronchi, and then to the alveoli in bronchioles.
- Muscle contractions cause the pressure changes inside the thorax that force air in and out of the lungs to ventilate them.
- Different muscles are required for inspiration and expiration because muscles only do work when they contract.

Applications and skills:

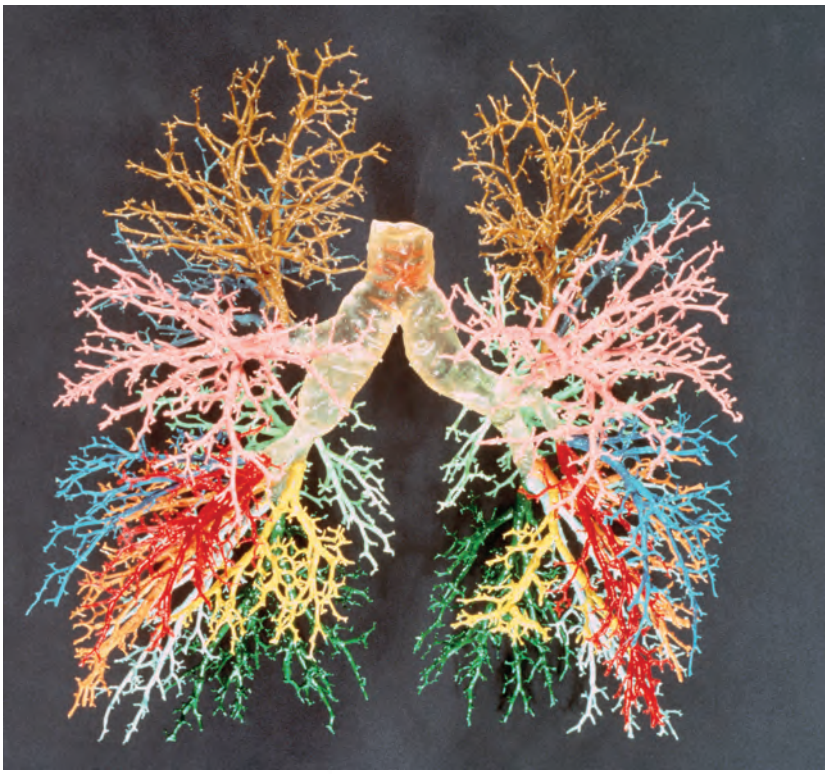
- Application: Causes and consequences of lung cancer.
- Application: Causes and consequences of emphysema.
- Application: External and internal intercostal muscles, and diaphragm and abdominal muscles, as examples of antagonistic muscle action.
- Skill: Monitoring of ventilation in humans at rest and after mild and vigorous exercise.

Guidance

- *Ventilation can either be monitored by simple observation and simple apparatus, or by data logging with a spirometer or chest belt and pressure meter. Ventilation rate and tidal volume should be measured, but the terms vital capacity and residual volume are not expected.*
- *Students should be able to draw a diagram to show the structure of an alveolus and an adjacent capillary.*

Overview of the respiratory system

Our lungs act in concert with our heart and blood vessels to ensure that body cells are well supplied with oxygen and are able to give up carbon dioxide. Most people



A resin cast image of airways in the lungs. The trachea divides into the right and left primary bronchi. Each primary bronchus continues to divide multiple times, leading to smaller and smaller bronchioles. You can see why the entire structure is sometimes called the 'bronchiole tree'.

never seriously consider why we need oxygen, but everyone knows that we do. The process that requires oxygen (and gives off carbon dioxide) is aerobic cell respiration. In brief, this is a biochemical pathway in which the chemical bonds within a glucose molecule are broken down sequentially to release energy. Much of this energy is then stored as molecules of adenosine triphosphate (ATP). In aerobic organisms, the process requires oxygen molecules, and each of the six carbons of a glucose molecule is given off as a carbon dioxide molecule.

Throughout our lives we continuously repeat the process of filling our lungs with air and then expelling that air. This is called ventilation. Even though the air we breathe is inside our lungs for only a short period of time, it is long enough for diffusion of gases to occur. Within the lungs are a multitude of small spherical air sacs called alveoli. Oxygen in the alveoli typically diffuses into the bloodstream, and carbon dioxide from the bloodstream typically diffuses into the alveoli. Each breath in and out maintains the concentration gradients that encourage diffusion of oxygen into and carbon dioxide out of the nearby capillary beds that are adjacent to the many alveoli making up the bulk of lung tissue.

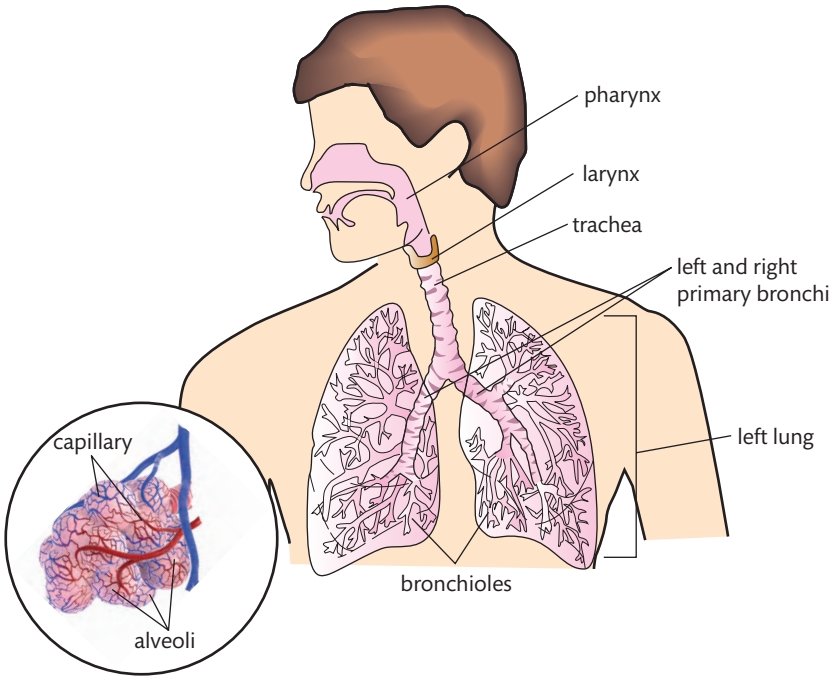
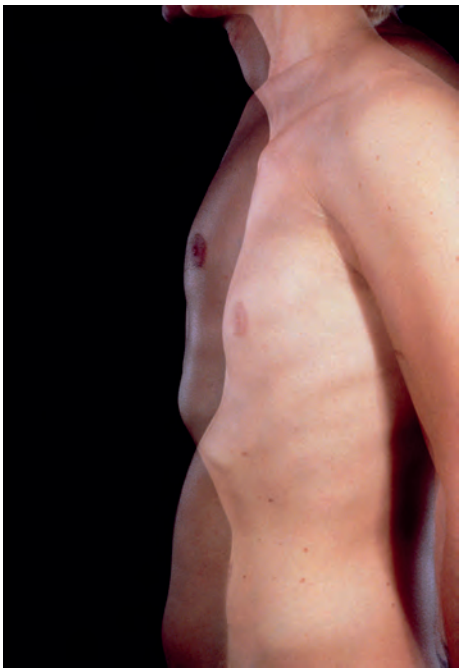


Figure 6.12 Air can enter the trachea from either the mouth or nasal passages. The inhaled air passes through the larynx (the voicebox with vocal cords) and then down the trachea. The trachea branches many times into multiple bronchioles. Finally the air reaches the small air sacs surrounded by rich capillary beds.

The mechanism of ventilation



A double-exposure photograph showing the position of the chest during inspiration and expiration. Inspiration is occurring when the chest/rib cage is in the raised position.

We breathe in and out continuously all our lives. Each time we take a breath, a fairly complex series of events occurs that we do not even think about as it is happening. The tissue that makes up our lungs is passive and not muscular, therefore the lungs themselves are incapable of purposeful movement. However, there are muscles surrounding the lungs, including the diaphragm, muscles of the abdomen, and the external and internal intercostal muscles (which surround your ribs).

The mechanism of breathing is based on the inverse relationship between pressure and volume (see Figure 6.13). Put simply, an increase in volume will lead to a decrease in pressure, and vice versa. Whatever pressure does, volume will do the opposite. Your lungs are located within your thoracic cavity (or thorax). The thoracic cavity is closed to the outside air. Your lungs have only one opening to the outside air, and that is through your trachea (via your mouth and nasal passages). Thus we need to consider the two environments that affect each other: one is the closed environment of the thorax, and the other is the internal environment of the lungs.

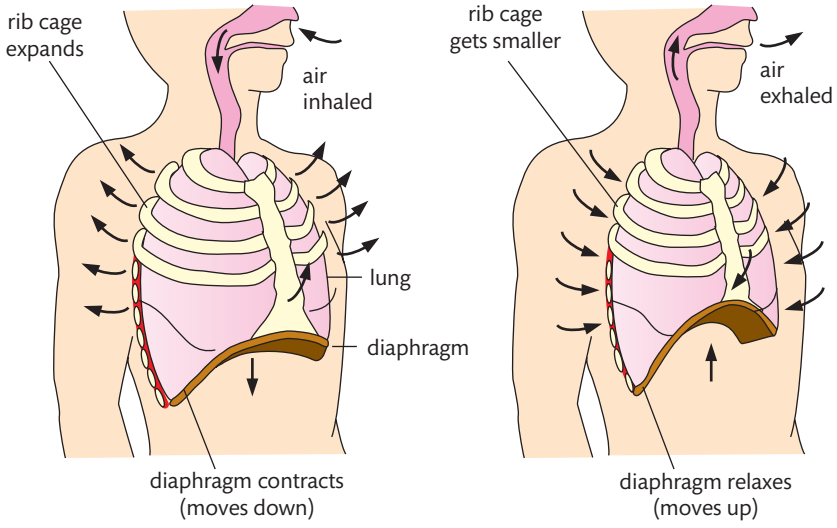


Figure 6.13 The mechanisms for inspiration and expiration (ventilation).

CHALLENGE YOURSELF

3 Create a list of steps that trace a single erythrocyte that begins in the capillary bed adjacent to an alveolus. Name the major blood vessels and heart chambers that the erythrocyte goes through until it returns to another capillary bed in the lungs. Hint: You will need to take the cell through the remaining pulmonary circuit, into a systemic circuit starting with the aorta, and then eventually back through the first portion of another pulmonary circuit.

Actions that lead to an inspiration (breathing in)

1 The diaphragm contracts, and at the same time the external intercostal muscles and one set of abdominal muscles help to raise the rib cage. Collectively, these actions increase the volume of the thoracic cavity.

CHALLENGE YOURSELF

4 List the five steps (in order) necessary for expiration, with the following as your starting point.
- The diaphragm relaxes and the internal intercostal muscles and a second set of abdominal muscles help to lower the rib cage. Collectively, these actions decrease the volume of the thoracic cavity.

Notice that different muscles are necessary for an inspiration versus an expiration. For example, the intercostal muscles are the muscles that are found between the ribs. There are two antagonistic sets of these muscles: external intercostals, which are used when breathing in, and the internal intercostals, which are used when breathing out.

2 Because the thoracic cavity has increased its volume, the pressure inside the cavity decreases. This leads to less pressure 'pushing on' the passive lung tissue.

3 The lung tissue increases its volume because there is less pressure exerted on it.

4 This leads to a decrease in pressure inside the lungs, also known as a partial vacuum.

5 Air comes in through your open mouth or nasal passages to counter the partial vacuum within the lungs, and fills the alveoli.

These steps are reversed for an expiration (breathing out).

All the steps become more frequent and exaggerated when you are exercising and thus breathing deeply. For example, the abdominal muscles and intercostal muscles achieve a greater initial thoracic volume. This leads to deeper breathing and thus more air moving into the lungs.

Monitoring ventilation in humans at rest and after mild and vigorous exercise

Safety alerts: Many schools and the IB Animal Experimentation policy require parent permission forms to be signed before any type of investigation of the pupils themselves is performed. If so, this must be completed well before the investigation begins.

Note: This investigation is best done as a whole class project with shared data sets.

This lab reinforces the concepts associated with changes in homeostatic mechanisms in the human body. Ventilation is the rate of breathing and is typically given as breaths min^{-1}. An increase in exercise predictably results in a greater use of oxygen and release of carbon dioxide to/from muscle tissue associated with the exercise.

Question

What is the correlation between ventilation rate and duration of exercise?

Hypothesis

Ventilation rate will be positively correlated with the increasing duration of a chosen exercise.

Planning steps necessary before beginning

Determine a safe exercise that can be accomplished by everyone that is happy to be a test subject. Typical examples might be walking up a flight of stairs or jumping jacks. Next, determine the maximum time duration that is both reasonable and safe for the exercise you have chosen. Hint: try to make it easy to subdivide your total duration time.

Summary of procedures

1. Choosing human subjects for experimentation is difficult as it is often not possible to account for comparable subjects based on criteria such as gender, age, body mass index (BMI) similarities, health, current level of activity (sports), and genetic background. You will probably have to make test groups from a very limited population of test subjects (e.g. your classmates). Try to set at least some limited criteria for test subjects. Try to make three to five test groups with as many test subjects in each group as possible. Five groups of five in each group would be ideal, but perhaps not realistic.
2. You will need baseline ventilation data for each individual test subject. Use a timer and count the number of breaths for a 20-second time period for each test subject. Record this as raw data and be sure to keep track of the identity of each person and his or her 20-second ventilation rate. The test subject can count his or her own breaths with someone else acting as a timer and recorder. An alternative is to use data logging hardware and software that is designed to measure ventilation rate and perhaps tidal volume (the volume of air in a single breath).
3. Individually, have each test subject do one, and only one, of the exercise durations you predetermined. Very soon after each subject has finished, take a 20-second count of his or her number of breaths and record that data, again making sure to keep track of who it is and the duration of his or her exercise. If the number of test subjects is very low, you may have to use one or more subjects for more than one exercise duration. If this is the case, make sure to allow as much recovery time between tests as possible.

Data-processing possibilities

- For each test subject, calculate a ventilation rate, expressed in breaths min^{-1}, for both the baseline and after-exercise raw data (the 20-second ventilation counts).
- For each test subject, calculate a percentage increase of ventilation rate, showing the increase after exercise compared with the baseline rate.
- Calculate the mean percentage increase for each group. Example: calculate the mean percentage increase for all the test subjects who did jumping jacks for 90 seconds.
- If your data set included at least five test subjects for each exercise duration, calculate the standard deviation of each of the means from the previous step.

Data-presentation possibilities

- Design and create a data table showing all the relevant raw data. Test subject numbers can be assigned instead of using names.
- Design and create a data table showing all the relevant processed data.
- Design and create a graph with exercise durations on the *x*-axis (with appropriate units) and mean percentage increases (% unit) on the *y*-axis.
- If the data set appears to be reasonably linear on your graph, draw a single best-fit line representing the overall data pattern.
- Add standard deviation error bars to each mean point plotted on your graph, and add a note to your graph that the error bars indicate standard deviation.

Gas exchange occurs in alveoli

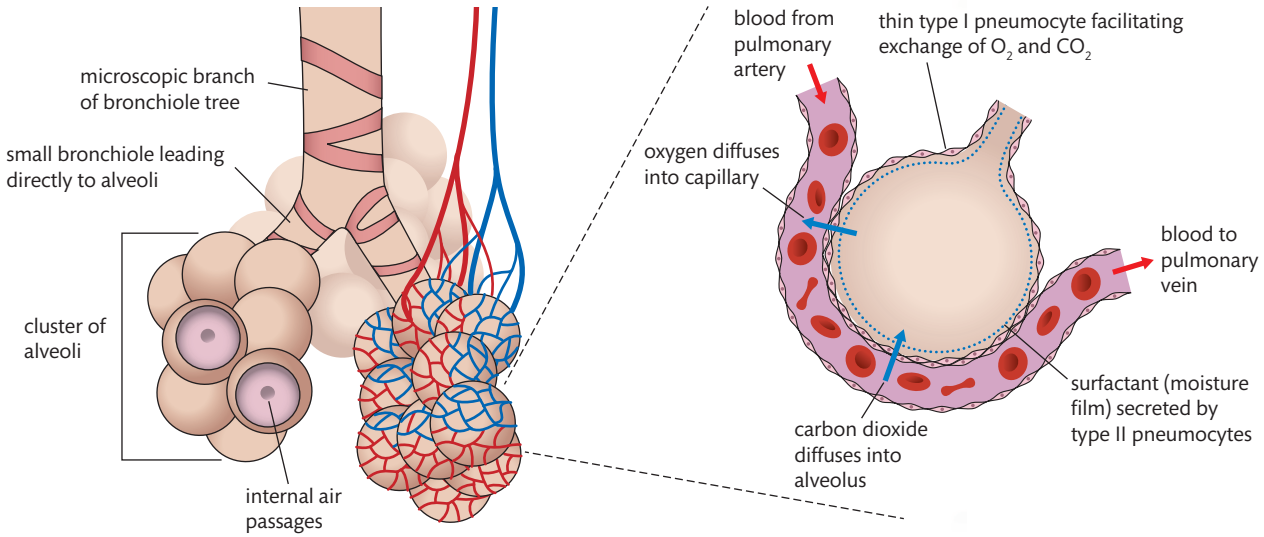


Figure 6.14 Microscopic view of a small area inside a human lung. Each cluster of alveoli is surrounded by a capillary bed for efficient gas exchange. The inset shows a sectioned drawing of a single alveolus and the structures that make gas exchange efficient.

When you take in air through your mouth or nasal passages:

- the air first enters your trachea
- then your right and left primary bronchi
- then smaller and smaller branches of the bronchi
- then very small branches called bronchioles
- then, finally, the air enters the small air sacs in the lungs called alveoli.

Alveoli in the lungs are found as clusters at the ends of the smallest bronchioles. In appearance they are very similar to a bunch of grapes. There are approximately 300 million alveoli in each of your lungs. Each cluster of alveoli has one or more surrounding capillary bed(s).

The blood entering these capillary beds comes from the right ventricle via the pulmonary arteries. As you will recall, blood within the pulmonary arteries is relatively low in oxygen and high in carbon dioxide. While this blood is in the capillary bed surrounding a cluster of alveoli, oxygen diffuses from the air in each alveolus through the membranes, which is only through two cells. The first of these is the single cell making up the structure of the alveolus, and the second is the single cell making up the wall of the capillary. Carbon dioxide diffuses in the opposite direction through the same two cells. As long as a person continues breathing, and refreshing the gases within the alveoli, the concentration gradients of these two gases will ensure diffusion of each gas in the direction that the body needs for healthy gas exchange.

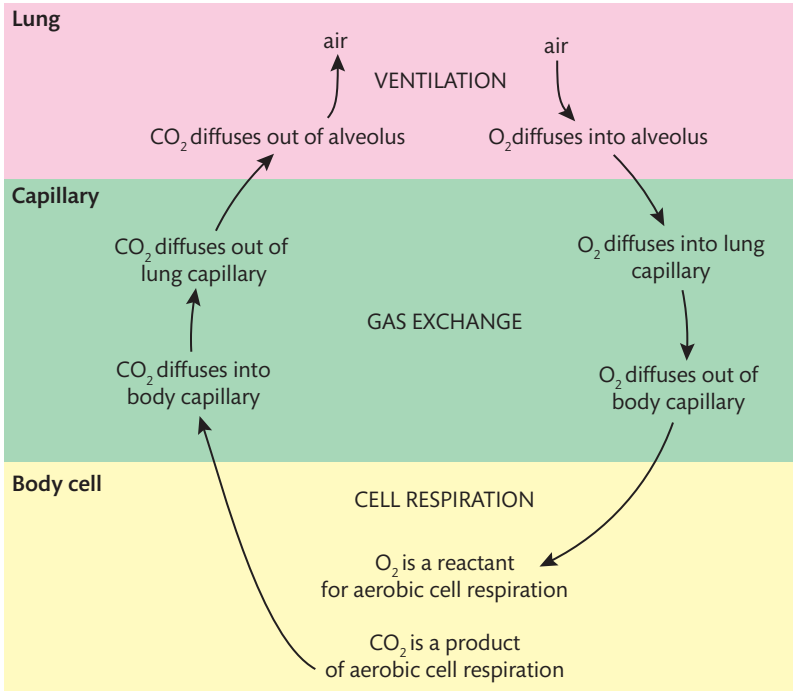


Figure 6.15 Relationship between ventilation, gas exchange and cell respiration.

Alveoli are composed of specialized cells called pneumocytes

An alveolus is an evolutionary marvel designed for efficient gas exchange. As mentioned above, one of the design features of an alveolus is that it is composed of a single layer of cells, to facilitate oxygen and carbon dioxide diffusion. This single cell layer is composed of two different types of cells called pneumocytes.

Type I pneumocytes

This type of alveolar cell is very thin but has a very large membrane surface area, making it well designed for diffusion. If damaged, these cells are incapable of mitosis for replacement.

Type II pneumocytes

This type of alveolar cell is cuboidal in shape and thus has relatively little membrane surface area. These cells produce and secrete a solution that acts as a surfactant. This reduces the surface tension of the moist inner surface of alveoli, and prevents the sides of the alveoli from sticking to each other. Type II pneumocytes are capable of mitosis for replacement of both types of alveolar cells if they are damaged.

Causes and consequences of emphysema

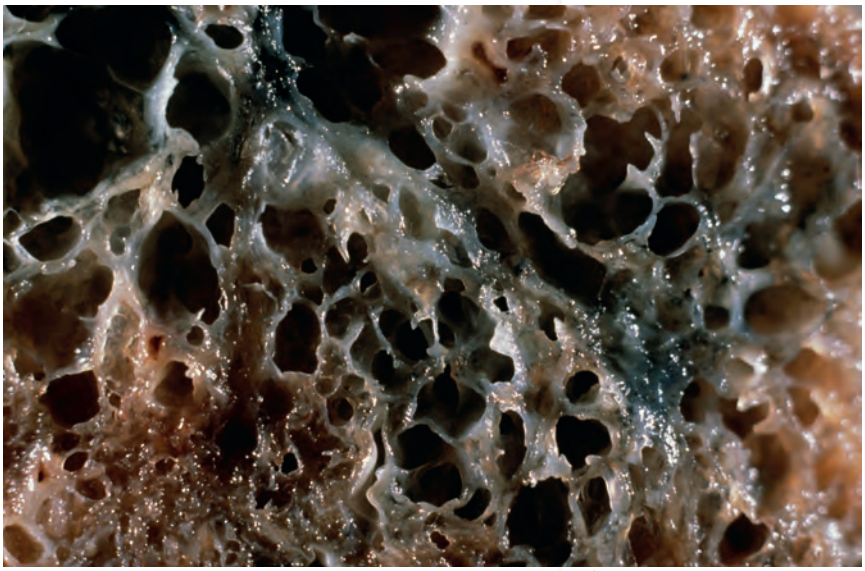
Emphysema is a disease whereby the alveoli in the lungs are progressively destroyed. The leading cause of emphysema is smoking. Emphysema is one of the diseases collectively known by the acronym COPD (chronic obstructive pulmonary disease). Emphysema is a chronic, slowly progressive disease that turns healthy alveoli into large, irregularly shaped structures with gaping holes. This reduces the surface area for gas exchange, and so less oxygen reaches the bloodstream. This explains the symptom described as 'shortness of breath'. At first, shortness of breath only occurs when the afflicted person does strenuous activity, but over time the inability to get sufficient gas exchange becomes constant.

Although long-term tobacco smoking is the leading cause of emphysema, there are other causes, including long-term exposure to the following:

- marijuana smoke
- fumes from manufacturing plants
- coal dust
- air pollution.

There is no cure for emphysema, but the progression of the disease can be slowed drastically with the cessation of smoking or exposure to other risk factors. To prevent emphysema, it is common sense not to even begin smoking, and to wear a protective mask when working around dust or chemical fumes.

The diagnosis of emphysema is often delayed because the symptoms develop slowly. People often associate the symptoms of emphysema with natural ageing, and people can initially find ways to compensate for their breathing problems.



Light microscope photograph of a section of lung taken from a diseased patient with emphysema. Notice the large gaping holes where healthy alveoli once were.

A better understanding of the causes of emphysema and lung cancer has led to massive campaigns to educate people about the dangers of smoking. In areas of the world where information concerning the dangers of smoking have been regularly and widely circulated, the percentage of people who smoke has declined.

Causes and consequences of lung cancer

Lung cancer is a cancerous growth that begins in the lungs. It is a cancer that is prone to spreading, a process called metastasizing. The brain, bones, liver, and adrenal glands are likely targets for lung cancer that has metastasized. The cancerous growth in the lungs takes over areas of healthy tissue areas that once provided a combination of bronchioles and alveoli. The larger the growth, the more the lung tissue becomes dysfunctional. Lung cancer can also result in internal bleeding in the lungs.

Lung cancer is caused by one or more carcinogen (a substance that is known to cause cancer) that enters the lung tissue and mutates cells into a cancerous growth. Sometimes the body is able to eliminate the early cancerous growth, but not always. More often than not, the carcinogen enters the lungs in cigarette smoke, although other fumes and substances have been known to be the source of the carcinogen.

The best treatment of lung cancer is achieved when the disease is diagnosed early in its progression. Lung cancer has a very high mortality rate.

Asbestos, once commonly used in building insulation products, is another carcinogen that can result in lung cancer. Many companies specialize in the safe removal of asbestos insulation from older buildings.

Once a company has freely admitted that its product is a risk to a consumer's health, does that admission eliminate the liability of that company in situations where the product does lead to poor health? This is the dilemma of current tobacco companies and the people that are addicted to their products.

TOK

Recent data supports a direct correlation between those countries and cultures that have shown a decrease in the number of people who smoke and a corresponding decrease in the incidence of lung cancer. Conversely, those areas of the world that are showing an increase in the number of people smoking are showing an increase in the incidence of lung cancer.

Exercises

11 Stopping smoking seems like such an easy, simple thing for people to do. Why do you think more people are not successful at stopping?

12 How are alveoli well adapted for efficient gas exchange?

13 Why are there two sets of muscles involved in ventilation (breathing)?

NATURE OF SCIENCE

Cooperation and collaboration between groups of scientists: biologists are contributing to research into memory and learning.

6.5 Neurones and synapses

Understandings:

- Neurones transmit electrical impulses.
- The myelination of nerve fibres allows for saltatory conduction.
- Neurones pump sodium and potassium ions across their membranes to generate a resting potential.
- An action potential consists of depolarization and repolarization of the neurone.
- Nerve impulses are action potentials propagated along the axons of neurones.
- Propagation of nerve impulses is the result of local currents that cause each successive part of the axon to reach the threshold potential.
- Synapses are junctions between neurones and between neurones and receptor or effector cells.
- When presynaptic neurones are depolarized they release a neurotransmitter into the synapse.
- A nerve impulse is only initiated if the threshold potential is reached.

Applications and skills:

- Application: Secretion and reabsorption of acetylcholine by neurones at synapses.
- Application: Blocking of synaptic transmission at cholinergic synapses in insects by binding of neonicotinoid pesticides to acetylcholine receptors.
- Skill: Analysis of oscilloscope traces showing resting potentials and action potentials.

Guidance

- *The details of structure of different types of neurones are not needed.*
- *Only chemical synapses are required, not electrical, and they can simply be referred to as synapses.*

The organization of the human nervous system

The brain and spinal cord comprise the central nervous system (CNS). These two structures receive sensory information from various receptors, and then interpret and process that sensory information. If a response is needed, some portion of the brain or spinal cord initiates a response that is called a motor response.

The cells that carry this information are called neurones. Sensory neurones bring information in to the CNS, and motor neurones carry response information to muscles.

Together, sensory neurones and motor neurones make up the peripheral nerves. A neurone is an individual cell that carries electrical impulses from one point in the body to another, and does so very quickly. When many individual neurones group together into a single structure, that structure is called a nerve. Think of a nerve as being like a

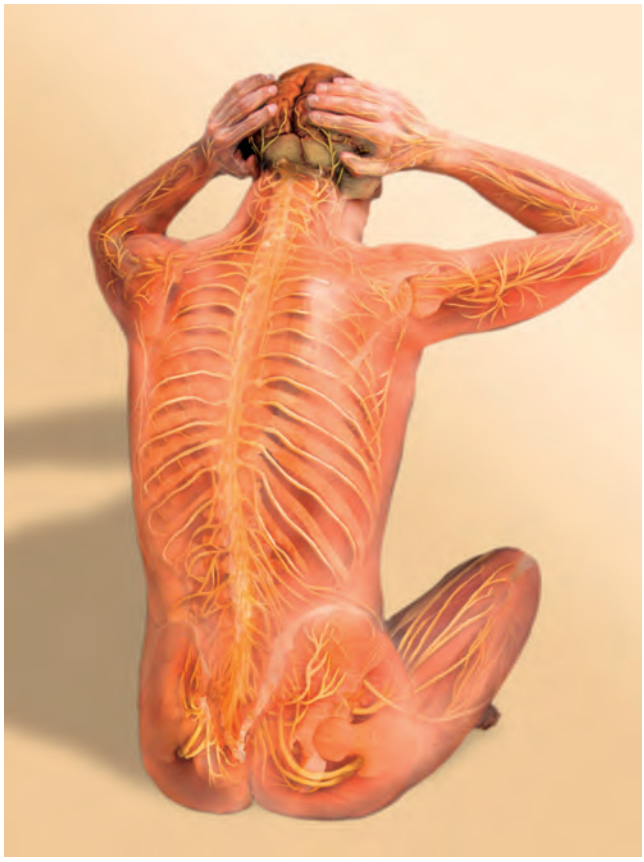
telephone cable: a protective sheath surrounding many individual wires. Each wire within that cable is like a neurone. The connection between the CNS and your body is made by two sets of nerves.

- Spinal nerves emerge directly from the spinal cord. They are mixed nerves, as some of the neurones within them are sensory and some are motor. There are 31 pairs of spinal nerves.
- Cranial nerves emerge from an area of the brain known as the brainstem. One well known example is the optic nerve pair, which carries visual information from the retina of the eyes to the brain. There are 12 pairs of cranial nerves.

Neurones

The cells that have been evolutionarily designed to transmit electrical impulses are called neurones. Neurones can be unusually long. In the human body, there are neurones that extend from the lower portion of the spinal cord all the way to the big toe: single cells that extend a distance of about 1 m! Of course, not all neurones are that long; in fact, some neurones are quite short.

Blue whales have some neurones that are approximately 25 m in length.



The central nervous system (CNS) consists of the brain and spinal cord. The peripheral nervous system (PNS) is made up of the nerves and branches that enter and leave the spinal cord and brainstem

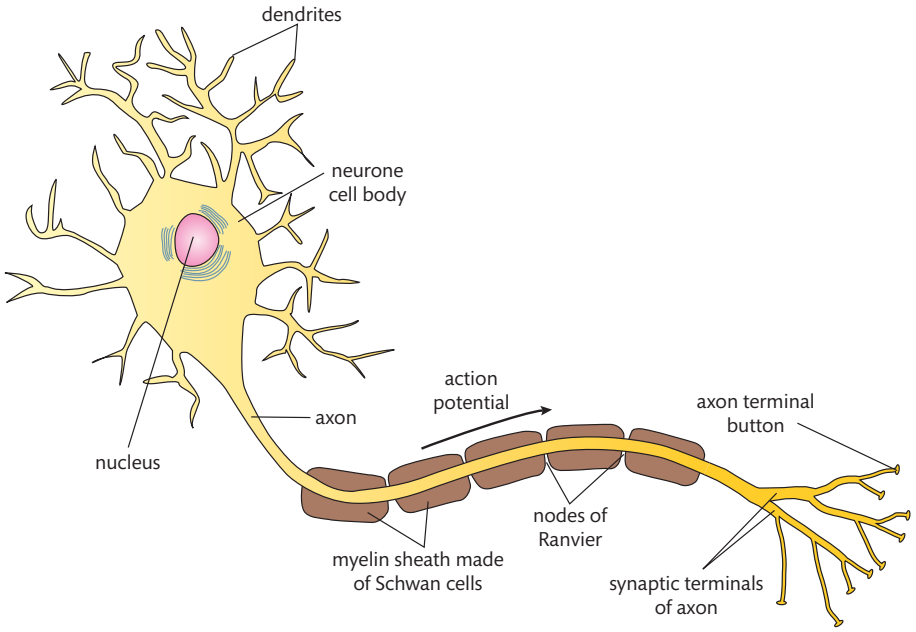
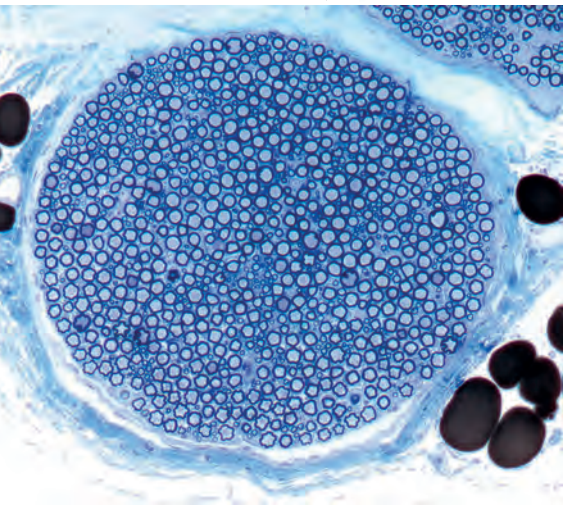


Figure 6.16 The structure of an individual neurone. The function of the myelin sheath and nodes of Ranvier are described on pages 302–303.

The three main subparts of a single neurone are its dendrites, cell body and axon. At the end of the axon are synaptic terminal buttons, which release chemicals called neurotransmitters that continue the impulse chemically to the next neurone(s) or possibly a muscle. An impulse is always carried from the dendrite end of a neurone along the membrane of the cell body down the axon, and results in a release of a neurotransmitter. The impulse does not travel in the opposite direction because neurotransmitter molecules cannot be released from the dendrite end of neurones, and the 'message' would simply stop at that point.



Light microscope photograph of a section of a nerve. The very large circle is the entire nerve, and each small circle within it is one of the axons of a neurone contained within that nerve.

What is a nerve impulse?

People often equate a nerve impulse to electricity. In some ways this is accurate, as a nerve impulse can be measured in the same way as electricity. For example, an action potential (or impulse) has a voltage, although the typical unit for this voltage is millivolts. In other ways, however, electricity and action potentials are very different. True electricity is a flow of electrons down a conductor; this is not the nature of an action potential. Let's look at what a nerve impulse actually is.

The term 'nerve impulse' is very misleading because a nerve does not carry an impulse; the individual neurones within the nerve are each capable of carrying the impulse. As axons of neurones are typically quite long, it is convenient to think of the conductor of a neurone impulse as the axon. The axons of neurones in some organisms (including humans) that have a very highly developed nervous system, have surrounding membranous structures collectively called the myelin sheath. The myelin sheath greatly increases the rate at which an action potential passes down an axon. In order to study the nature of an action potential, it is best to study an axon that does not have a myelin sheath, otherwise known as a non-myelinated neurone.

Resting potential: not currently sending an impulse

Let's look first at what an axon of a neurone is like when it is not sending an impulse. The time period during which an area of a neurone is ready to send an action potential, but is not actually sending one, is called the resting potential, and this area of the neurone is said to be polarized. The resting potential is created by the active transport of sodium ions (Na^+) and potassium ions (K^+) in two different directions. The vast majority of the sodium ions are actively transported out of the axon cell into the intercellular fluid, and the majority of the potassium ions are transported into the cytoplasm. This active transport of sodium and potassium in opposite directions is an active transport mechanism called the sodium–potassium (Na/K) pump. The Na/K pump works by transporting three sodium ions 'out' for every two potassium ions 'in'. In addition, there are negatively charged organic ions permanently located in the cytoplasm of the

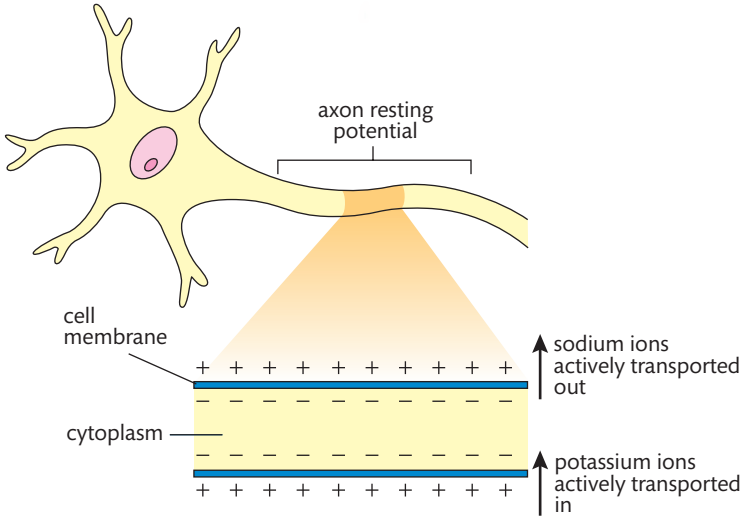


Figure 6.17 A neurone axon at resting potential. Think of the axon as a three-dimensional 'tube', and thus the ion movements shown are occurring all around the tube.

axon. The net result of the position of the charged ions leads to a net positive charge outside the axon membrane (positive in relation to the inside) and a net negative charge inside the axon membrane (see Figure 6.17).

Depolarization: sending an impulse

An action potential is often described as a self-propagating wave of ion movements in and out of the neurone membrane. The movement of the ions is not along the length of the axon, but instead consists of ions diffusing from outside the axon to the inside, and from inside the axon to the outside. The resting potential requires active transport (the Na/K pump) to set up a concentration gradient of both sodium and potassium ions. As sodium ions are actively transported to the outside of the membrane, they diffuse in when a channel opens. This diffusion of sodium ions is the 'impulse' or action potential, and results in the inside of the axon becoming temporarily positive in relation to the outside. It is a nearly instantaneous event that occurs in one area of an axon, and is also called a depolarization. This depolarized area of the axon then initiates the next area of the axon to open up the channels for sodium, and thus the action potential continues down the axon. This is the self-propagating part of an action potential; once you start an impulse at the dendrite end of a neurone, that action potential will self-propagate to the axon end of the cell, where the synaptic terminals are located.

Each action potential must reach a minimum threshold in order to be self-propagated. This begins at the first receptor neurone that began the chain of events. A receptor neurone is a neurone that is modified to begin the sequence of events by transducing (converting) a physical stimulus of some kind into the first action potential. For example, some of the cells that make up the retina of your eyes are receptor cells. Each type of retinal cell has a minimum physical stimulus magnitude that is required in order to begin the impulse. For some retinal cells this is a minimum intensity of light. If that minimum intensity is not reached, no action potential begins. If the minimum is reached, an action potential is initiated and begins to self-propagate. There is no such thing as a strong impulse or a weak impulse: if the minimum threshold for that type of receptor is reached, an impulse begins. When a nerve impulse is being self-propagated along a neurone, that is happening because each successive area of the neurone membrane has reached its threshold and is causing the next area of the membrane to also reach its threshold.

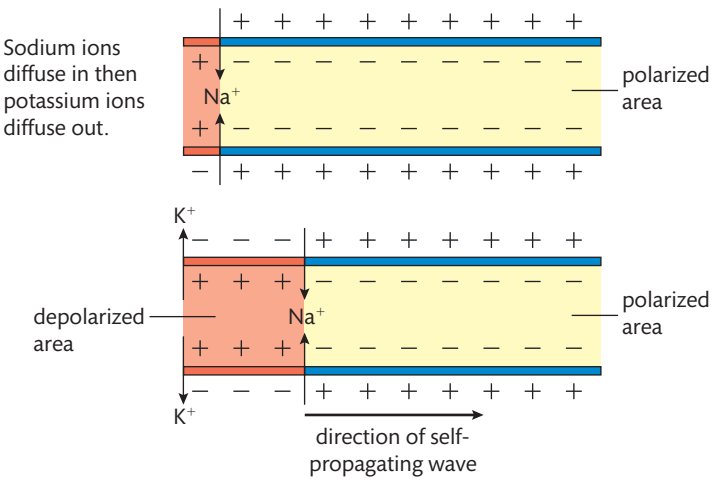


Figure 6.18 A neurone axon during and shortly after a depolarization.

Typically we are not aware of single impulses that reach our brain. If we sense a small amount of pressure on some area of our skin, it is because a few pressure receptors in that area have reached their threshold. If we feel a greater pressure, it is because the pressure has caused even more receptors in that area to reach their minimum threshold.

Nerve impulses are action potentials propagated along the axons of neurones.

Repolarization: return to the resting potential

Neurones do not send just one action potential; one neurone may send dozens of action potentials in a very short period of time. When one area of an axon has opened a channel to allow sodium ions to diffuse in, that area cannot send another action potential until ions have been restored to the positions characteristic of the resting potential. Diffusion cannot do this, thus active transport is required to pump ions to their resting potential positions.

If you recall from earlier, a depolarization is when sodium ions diffuse through the axon membrane from outside to inside. This means that, for a very short period of time, both sodium ions and potassium ions are inside together (this is why the inside of the membrane becomes positive relative to the outside). You may also recall that the active transport mechanism that resulted in the resting potential positions of sodium and potassium was the Na/K pump. This pump only works by moving sodium in one direction and potassium in the other direction across the membrane. Thus, immediately following an action potential (depolarization), membrane proteins open to potassium ions and allow them to diffuse out of the axon. This is the first step of repolarization because it separates many of the sodium and potassium ions on different sides of the membrane. The problem is that these two ions are on the opposite side of the membrane in relation to where they need to be for the resting potential. The good news is that they are now in a position that allows the Na/K pump to once again begin actively transporting them across the membrane at the ratio characteristic of this pump (three sodium ions pumped out for every two potassium ions pumped in). This entire series of events, beginning with potassium ions diffusing out of the localized area of the membrane, is called repolarization. All of this is necessary for that local area of the membrane to be ready to send another impulse.

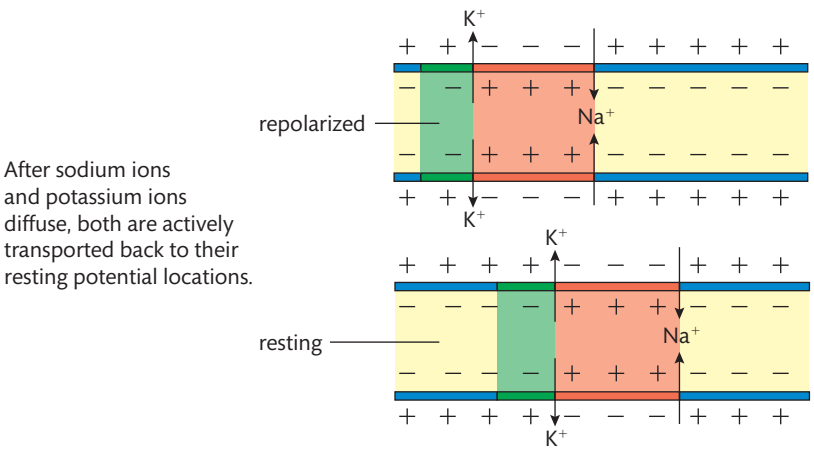


Figure 6.19 Return to the resting potential.

Saltatory conduction by neurones that have a myelin sheath

Many neurones of an organism with an advanced nervous system have axons with a myelin sheath; they are said to be myelinated. As an axon is like a long fibre, these axons are sometimes referred to as myelinated fibres. The myelin sheath is actually a series of cells, called Schwann cells, that have each wrapped themselves around the axon multiple times, creating multiple layers of the same cell membrane. The Schwann cells are spaced evenly along any one axon, with small gaps between them; these gaps are called nodes of Ranvier.

The term saltatory comes from the Latin word 'saltare', which means to hop or leap.

Saltatory conduction is the term used to describe the phenomenon whereby an action potential of myelinated axons skips from one node of Ranvier to the next as the impulse progresses along the axon towards the synaptic terminals. In other words, the action potential does not have to undergo the time-consuming and energy-expensive ion movements in the area of the membrane underneath the myelin material. The reason for this is that the myelin sheath acts as an insulator, preventing charge leakage through the membrane. The cytoplasm within the axon is electrically conductive, which allows the electrical potential to skip from one node of Ranvier to the next. The advantage of this is two-fold.

- The impulse travels much faster compared with an impulse in non-myelinated fibres, because the in/out ion movements characteristic of an impulse take time, and saltatory conduction allows areas of the membrane to be skipped. This is very important for the efficient neural processing characteristic of organisms with a high functioning nervous system.
- Less energy in the form of ATP is expended for the transmission of impulses, as the only locations where the Na/K pump needs to re-establish resting potentials is at the nodes of Ranvier.

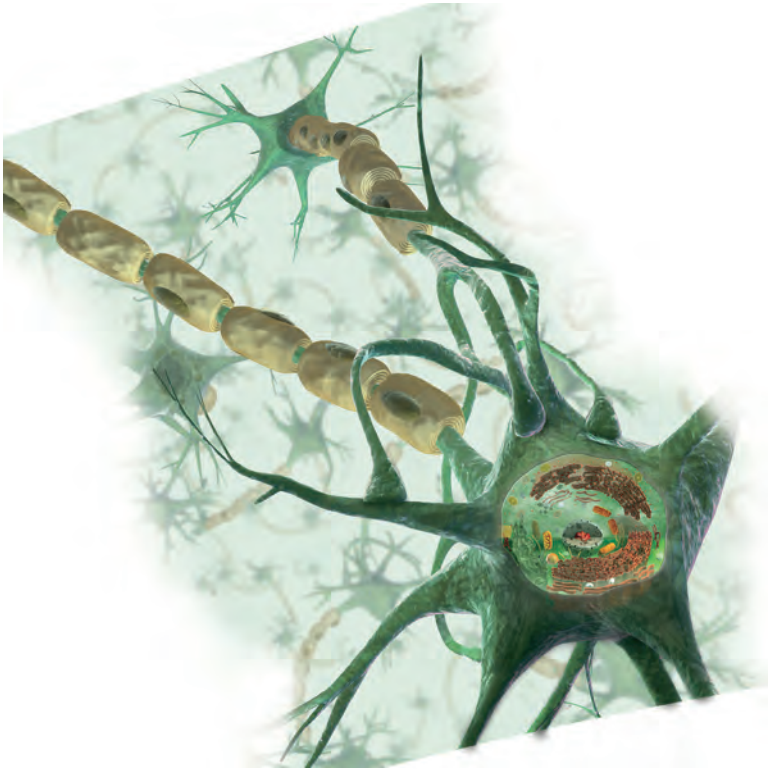
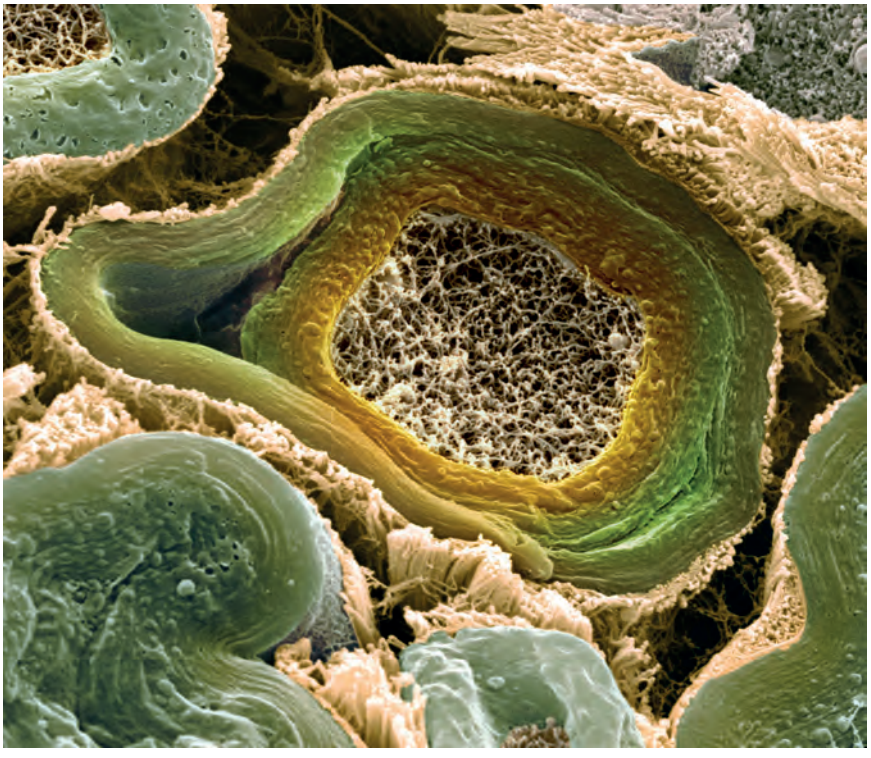
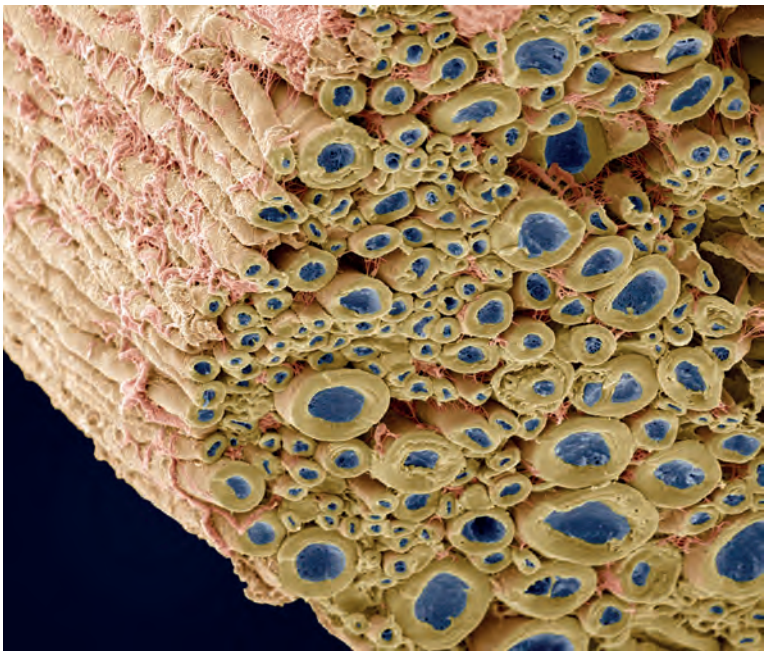


Illustration showing neurones with myelinated axons and nodes of Ranvier.



A false-colour SEM of a sectioned neurone with a myelin sheath. The axon is the centre beige area, and the myelin sheath is the surrounding yellow and green area.



A false-colour SEM of a nerve (bundle of neurones) with myelin sheaths. The blue colour shows the axons, and the surrounding yellow is the myelin sheath of each axon.

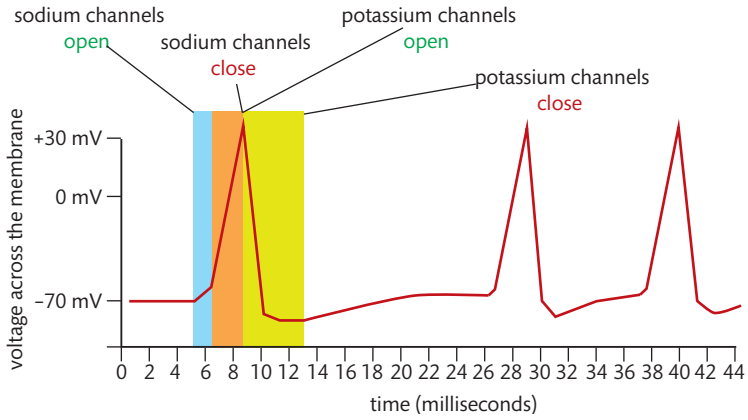


Figure 6.20 A graph showing the voltage changes across the membrane of an axon for three nerve impulses. Some of the important events are labelled on one of these impulses.

CHALLENGE YOURSELF

5 Use Figure 6.20, showing the change in voltage for a neurone sending impulses down its axon, to answer the following questions.

- **(a)** If each spike on this graph shows an impulse somewhere in the middle of an axon, what event must have just occurred in the area of the axon just preceding this one?
- **(b)** If the axon shown is myelinated, where along the axon did these voltage changes occur?
- **(c)** If this graph shows an impulse somewhere in the middle of an axon, and this is a myelinated fibre, what area of the axon will next undergo an action potential?
- **(d)** Where along the *x*-axis of the graph would the sodium–potassium pump be beginning to work to re-establish a resting potential?
- **(e)** What do you think would happen if discrete sensory information from a receptor was being received repeatedly at a rate faster than about 5 milliseconds apart?

Synapses: chemical communication between neurones

When one neurone communicates with another, the communication is chemical and occurs where two (or more) neurones adjoin each other in an area called a synapse. The two neurones always align with each other so that the axon's synaptic

terminals of one neurone adjoin the dendrites of another neurone. The chemical, called a neurotransmitter, is always released from the synaptic terminal buttons of the first neurone, and typically results in a continuation of the impulse when the neurotransmitter is received by the dendrites of the second neurone. The neurone that releases the neurotransmitter is called the presynaptic neurone, and the receiving neurone is called the postsynaptic neurone.

At the distal end of axons, as part of the synaptic terminals, are swollen membranous areas called terminal buttons. Within these terminal buttons are many small vesicles filled with the chemical neurotransmitter. There are many examples of neurotransmitters; a very common example in humans is acetylcholine.

When an action potential reaches the area of the terminal buttons, it initiates the following sequence of events (see Figure 6.21).

1. Action potential results in calcium ions (Ca^{2+}) diffusing into the terminal buttons.
2. Vesicles containing the neurotransmitter fuse with the plasma membrane and release the neurotransmitter.
3. The neurotransmitter diffuses across the synaptic gap (or cleft) from the presynaptic neurone to the postsynaptic neurone.
4. The neurotransmitter binds with a receptor protein on the postsynaptic neurone membrane.
5. This binding results in an ion channel opening and sodium ions diffusing in through this channel.
6. This initiates the action potential to begin moving down the postsynaptic neurone because it is now depolarized (the action potential is now self-propagating).
7. The neurotransmitter is degraded (broken into two or more fragments) by a specific enzyme(s) and neurotransmitter is released from the receptor protein.
8. The ion channel closes to sodium ions.
9. Neurotransmitter fragments diffuse back across the synaptic gap to be reassembled in the terminal buttons of the presynaptic neurone (often called reuptake).

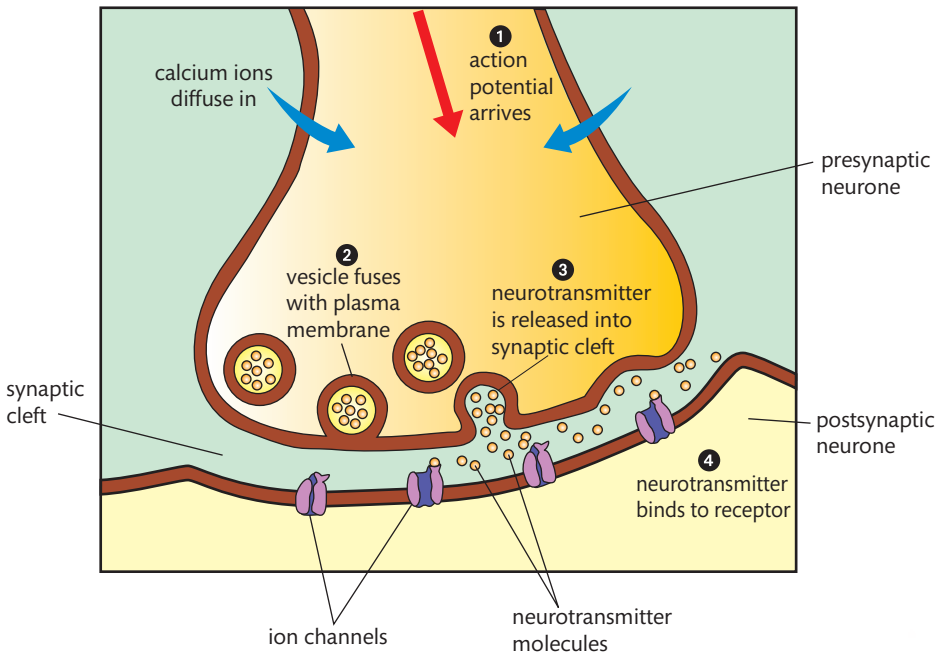
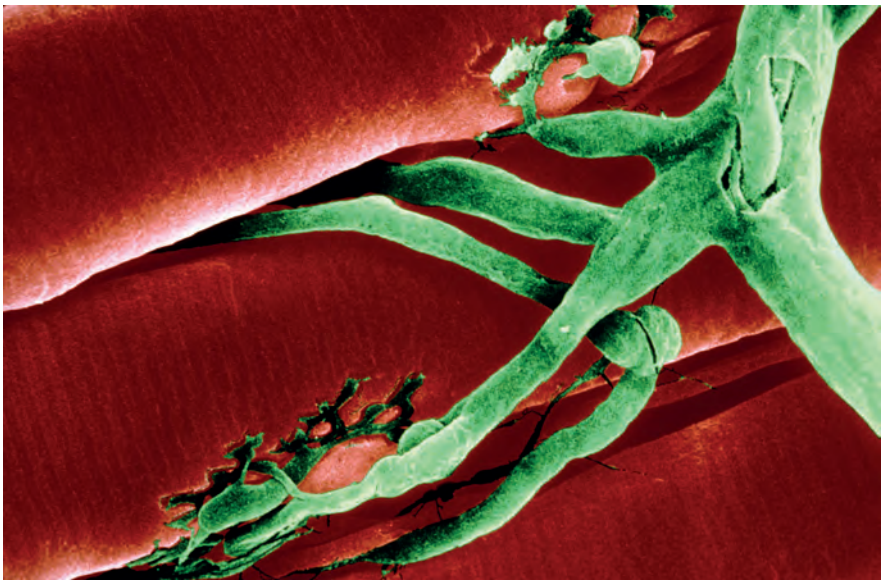


Figure 6.21 The mechanism of synaptic transmission.

Many mental disorders are associated with imbalances of certain neurotransmitters within the brain. There are approximately 50 different neurotransmitters that have been identified as active in the human brain. An imbalance of just one can result in conditions such as schizophrenia or severe depression. A large number of pharmaceuticals have been developed to treat these conditions based on our knowledge of how synapses and neurotransmitters work.

Synapses can also occur where a motor neurone adjoins muscle tissue. This type of synapse is called a motor end plate or neuromuscular junction. The mechanism for this type of synapse is almost the same as a neurone–neurone synapse, although the end result leads to the muscle undergoing a contraction. Another place for a synapse is between a receptor neurone (cell) of the nervous system and the first sensory neurone.



Synapses can be between a receptor and first sensory neurone, or between two neurones, or between a motor neurone and muscle. This false-colour SEM shows a synapse between a neurone (green) and a muscle fibre (red).

Early studies of neonicotinoid pesticides suggested that they were relatively safe from an ecological viewpoint. More recent studies are showing some possible links to the 'colony collapse syndrome' being experienced by honeybee colonies. Each country must consider the mounting evidence, but chemicals in our environment have ways of crossing international borders through water, air, and many other means. If neonicotinoids are shown to cause damage to honeybee colonies, an international effort to curtail or stop their use will be necessary.

A new class of insecticides based on blocking synaptic transmission

Neonicotinoid insecticides are a relatively new class of insecticide that are chemically similar to nicotine. This type of insecticide works by binding to postsynaptic receptors that normally accept the neurotransmitter acetylcholine. When acetylcholine binds to the receptor protein, the result is the normal continuation of the action potential along the postsynaptic neurone. When neonicotinoid molecules bind to the same receptor proteins, the action potential is not propagated. In addition, the neonicotinoid molecules are not broken down by the enzyme acteylcholinesterase and thus the receptor becomes permanently blocked. This leads to a paralysis of the affected insect, and eventually death.

NATURE OF SCIENCE

The fields of psychology, chemistry, biology, and medicine all combine to contribute to our knowledge of memory and learning. One of the many complications for research on memory and learning is the sheer complexity of the human brain. Often, complex biological systems are best studied by using simpler 'models' that represent the more complex activity.

Biologists often use invertebrates that have a simpler nervous system compared with humans and other vertebrates. One interesting invertebrate is a sea snail called *Aplysia*. This marine snail can be stimulated to retract its siphon when it is touched, as part of its defence mechanism. The snail can learn from experience, and can keep its siphon protected for a longer period of time after being given a chance to learn. In addition, repeated touching of the siphon leads to a greater number of synapses between neurones in the very simple brain of *Aplysia*. This can be observed and documented because *Aplysia* has very few, but very large, neurones that can be easily seen. Use the hotlinks at the end of this section to see a video of *Aplysia* and this research.

Exercises

14 Explain the advantage that myelinated neurones have over non-myelinated neurones.

15 Individual neurones do not send action potentials with different 'strengths'. An action potential is either propagated (sent) or it is not. What is the term that describes the minimum electric potential necessary to propagate an impulse?

16 Arrange these events in the correct sequence to represent synaptic transmission.

(a) Binding of neurotransmitter to receptor protein on postsynaptic neurone.
(b) Enzyme degrades neurotransmitter.
(c) Ca^{2+} ions enter synaptic (terminal) buttons.
(d) Reuptake of neurotransmitter fragments.
(e) Neurotransmitter diffuses across synaptic gap.
(f) Na^{+} ions diffuse into postsynaptic neurone channels.

To learn more about *Aplysia*, go to the hotlinks site, search for the title or ISBN and click on Chapter 6: Section 6.5.

6.6 Hormones, homeostasis, and reproduction

Understandings:

- Insulin and glucagon are secreted by β and α cells in the pancreas, respectively, to control blood glucose concentration.
- Thyroxin is secreted by the thyroid gland to regulate the metabolic rate and help control body temperature.
- Leptin is secreted by cells in adipose tissue and acts on the hypothalamus of the brain to inhibit appetite.
- Melatonin is secreted by the pineal gland to control circadian rhythms.
- A gene on the Y chromosome causes embryonic gonads to develop as testes and secrete testosterone.
- Testosterone causes prenatal development of male genitalia and both sperm production and development of male secondary sexual characteristics during puberty.
- Oestrogen and progesterone cause prenatal development of female reproductive organs and female secondary sexual characteristics during puberty.
- The menstrual cycle is controlled by negative and positive feedback mechanisms involving ovarian and pituitary hormones.

Applications and skills:

- Application: Causes and treatment of Type I and Type II diabetes.
- Application: Testing of leptin on patients with clinical obesity and reasons for the failure to control the disease.
- Application: Causes of jet lag and use of melatonin to alleviate it.
- Application: The use in IVF of drugs to suspend the normal secretion of hormones, followed by the use of artificial doses of hormones to induce superovulation and establish a pregnancy.
- Application: William Harvey's investigation of sexual reproduction in deer.
- Skill: Annotate diagrams of the male and female reproductive system to show names of structures and their functions.

Guidance

- *The roles of FSH, LH, oestrogen, and progesterone in the menstrual cycle are expected.*
- *William Harvey failed to solve the mystery of sexual reproduction because effective microscopes were not available when he was working, so fusion of gametes and subsequent embryo development remained undiscovered.*

NATURE OF SCIENCE

Developments in scientific research follow improvements in apparatus: William Harvey was hampered in his observational research into reproduction by lack of equipment. The microscope was invented 17 years after his death.

Homeostasis

The human body typically stays within certain limits for many physiological variables. This is referred to as homeostasis. Here are some representative physiological variables:

- blood pH
- blood carbon dioxide concentration
- blood glucose concentration
- body temperature
- water balance within tissues.

Each of these variables has an expected value or set point that is considered to be normal for homeostasis. For example, you often hear that our internal body temperature is 37°C (98.6°F). However, there is an inevitable fluctuation around this exact temperature, depending on what a person has been doing, for example exercising or being out in very cold weather.

The physiological processes that bring a value back towards to a set point are called negative feedback mechanisms. Think of negative feedback control as working like a thermostat. The thermostat triggers one set of actions that is required when a value rises above its set point, and another set of actions when a value falls below its set point. Thus negative feedback functions to keep a value within the narrow range that is considered normal for homeostasis.

There are two main categories of glands. Exocrine glands are those that produce a secretion (enzyme, saliva, etc.) that is carried to a nearby, specific, location via a duct. Endocrine glands always produce one or more hormones, and these hormones are always secreted into the blood for distribution throughout the body.

The nervous and endocrine systems work cooperatively in order to ensure homeostasis. Many of the homeostatic mechanisms initiated by your nervous system are under the control of your autonomic nervous system. The endocrine system consists of numerous glands that produce a wide variety of hormones. Each hormone is transported by the bloodstream from the gland where it is produced to the specific cell types in the body that are influenced by that particular hormone.

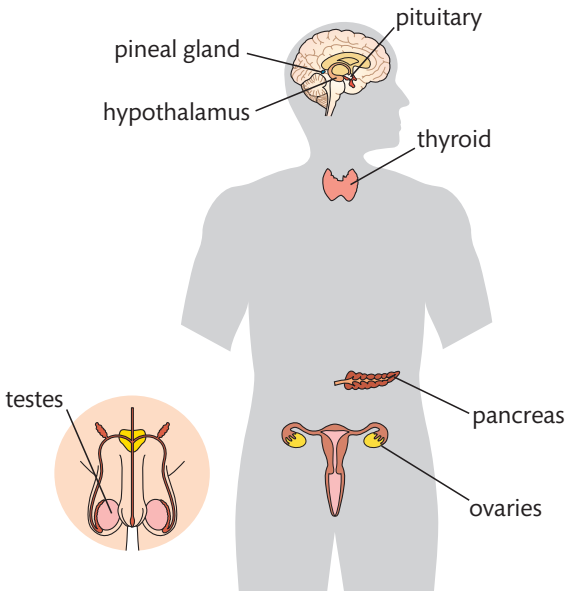


Figure 6.22 Some of the more common endocrine glands within the human body. Each of these glands produces one or more hormones that are secreted into the bloodstream and are carried to target tissues within the body. Target tissues are those cells that are influenced by any one hormone.

Selected hormones and their functions

Each hormone has a specific gland that produces and secretes the hormone into nearby capillary beds for distribution to body cells. Not all body cells are influenced by any one hormone: those cells that are influenced by a hormone are called the target

tissue(s) of the hormone. Some hormones (e.g. leptin) have very specific and limited target tissues, while others (e.g. insulin) have a broad range of target tissues.

Thyroxin

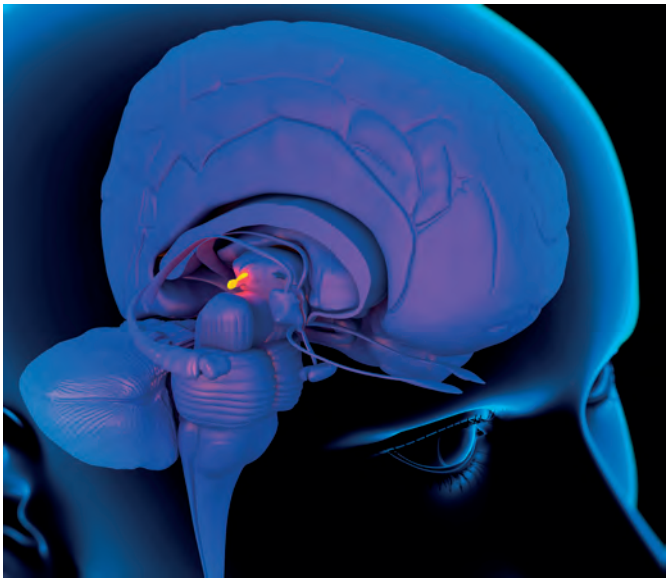
The gland that produces and secretes thyroxin is a 'butterfly'-shaped gland located in your neck called the thyroid gland. Thyroxin is created from an amino acid and iodine, and exists in two forms, one called T4 and the other called T3. The numbers indicate the number of iodine atoms within the structure. Both T3 and T4 enter the target cells (almost all cells in the body), where the T4 form is typically converted to the T3 form. The T3 form enters the nucleus of the cell and acts as a transcription regulator, leading to an increase in messenger (m)RNA and thus a resultant increase in proteins. Ultimately these proteins lead to an increase in the metabolism of the cell. Thus a cell under the influence of thyroxin will have a greater need for oxygen and other indicators of an increased metabolic rate. Someone who secretes too much thyroxin is said to have hyperthyroidism, and someone who secretes too little is said to have hypothryroidism. Both conditions can have serious symptoms.

In addition to increasing the metabolic rate, thyroxin helps to regulate internal body temperature. An increase in metabolic rate produces more heat from the increased chemical reactions that are occurring. Therefore an increase in thyroxin will lead to an increase in body temperature, and vice versa.

As mentioned, the synthesis of thyroxin requires iodine. People whose diets are deficient in iodine can develop hypothyroidism. Over time, with a deficiency of iodine, the thyroid gland tries to compensate by growing larger, and becomes markedly visible as it swells in size. An enlarged thyroid growth is called a goitre. Iodine deficiency has in fact become very rare in modern humans because most table salt has iodine added to it, thus it is sold as 'iodized salt'.

Leptin

Leptin is a hormone that is produced by adipose (fat) tissue in the body. The more fat stored in the body, the more leptin is produced and secreted into the bloodstream. Leptin's target cells are in the hypothalamus of the brainstem. Under ideal circumstances, leptin has the effect of lowering your appetite. Evolutionarily, the logic is simple: if someone has enough fat reserves, that person does not need to eat as much anymore. Unfortunately that simple logic doesn't always hold true, as evidenced by the very large incidence of obesity in modern society today. People who are obese are known to have a greater level of leptin circulating in their bloodstream. Researchers are working on why they appear to have become 'desensitized' to this high level of the appetite-controlling hormone. Some researchers have suggested that the function of leptin is related to increasing appetite when fat reserves are low, but not as an appetite suppressant when fat reserves are high.



The pineal gland highlighted in a sectioned view of the human brain. The right cerebrum and a portion of the brainstem has been removed in order to show the location of this small gland associated with sleep/wake cycles.

Melatonin

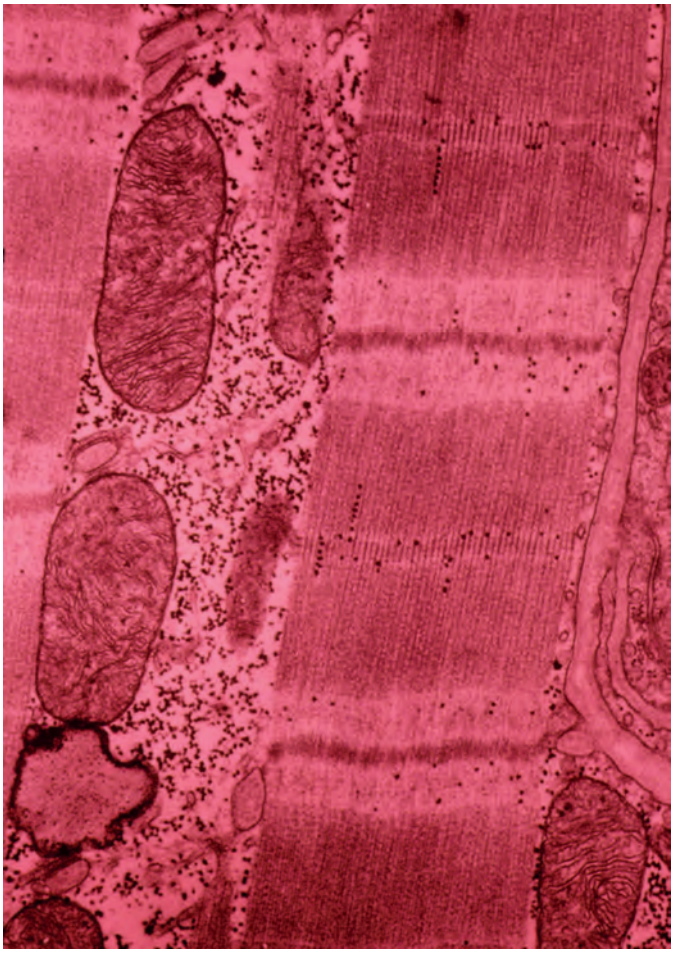
Deep within your brain is a very small gland called the pineal gland. Many animals use their pineal gland to help regulate their daily 24-hour cycle of activity, called the circadian rhythm. The hormone produced and secreted from the pineal gland is called melatonin. The pineal gland produces very little melatonin during the daytime, and is at peak production after dark, with maximum production occurring between 2 a.m. and 4 a.m. The natural circadian rhythm is altered when a person alters his or her period of exposure to light over a short period of time, especially when coupled

with a disruption of their normal sleep schedule. This is what is typically called 'jet lag', produced when a person travels through several time zones in a short period of time. Similar disorientation symptoms can be felt by people who work temporary night shifts or have other irregular time patterns of sleep versus being awake. Many people report a decline in the disorienting effects of jet lag by taking melatonin pills until their own circadian rhythm has naturally reset.

Insulin and glucagon help regulate glucose levels

Insulin and glucagon are hormones that are both produced and secreted by the pancreas. In addition, they are both involved in the regulation of blood glucose levels. Cells rely on glucose for the process of cell respiration. Cells never stop cell respiration and thus are constantly lowering the concentration of glucose in the blood. Many people eat three or more times a day, including foods containing glucose, or carbohydrates that are chemically digested to glucose. This glucose is absorbed into the bloodstream in the capillary beds of the villi of the small intestine, and thus increases the blood glucose level. So one factor that causes our blood glucose levels to fluctuate is simply that our blood does not receive constant levels of glucose. The increase and decrease in blood glucose levels goes on 24 hours a day, every day of your life. However, even though blood glucose is expected to fluctuate slightly above and below the homeostatic normal level, it must be maintained reasonably close to the body's set point for blood glucose level, and negative feedback mechanisms ensure this.

TEM of a cardiac muscle cell. Granules of glycogen can be seen as small black dots. Glucose is stored as glycogen in liver and muscle cells, and later can be reconverted back to glucose. Two mitochondria (ellipses) can be seen on the left.



In the intestinal villi, the glucose travels through a multitude of capillaries, small venules, and veins into the hepatic portal vein, which takes the blood to the liver. The glucose concentration in the hepatic portal vein varies depending on the time of your last meal and the glucose content of the food you ate. The hepatic portal vein is the only major blood vessel in the body in which blood levels fluctuate to a large degree. All other blood vessels receive blood after it has been processed by liver cells called hepatocytes. Hepatocytes are triggered into action by the two pancreatic hormones, insulin and glucagon. These two pancreatic hormones are antagonistic: they have opposite effects on blood glucose concentration.

What happens when blood glucose begins to rise above the set point?

In the pancreas there are cells known as β (beta) cells that produce the hormone insulin. Insulin is then secreted into the bloodstream and, because all body cells communicate chemically with blood, all cells are exposed to insulin. Insulin's effect on body cells is to open protein channels in their plasma membranes. These channels allow glucose to diffuse into the cell by the process known as facilitated diffusion.

There is another important effect attributed to insulin. When blood that is relatively high in glucose enters the liver by the hepatic portal vein, insulin stimulates the hepatocytes to take in the glucose (a monosaccharide) and convert it to glycogen (a polysaccharide). The glycogen is then stored as granules in the cytoplasm of the hepatocytes. The same effect occurs in muscles (see the TEM on the previous page).

The two effects of insulin both have the same ultimate result, which is to lower the glucose concentration in the blood or, to put it more simply, to reduce blood glucose.

What happens when blood glucose begins to fall below the set point?

The blood glucose level typically begins to drop below the set point when someone has not eaten for many hours or exercises vigorously for a long time. In either situation, the body needs to use the glycogen made and stored by the liver (and muscle cells). Under these circumstances, α (alpha) cells of the pancreas begin to produce and secrete the hormone glucagon. The glucagon circulates in the bloodstream and stimulates hydrolysis of the granules of glycogen stored in hepatocytes and muscle cells; the hydrolysis produces the monosaccharide glucose. This glucose then enters the bloodstream. The ultimate effect is to increase the glucose concentration in the blood or, to put it more simply, to increase blood glucose (see Figure 6.23).

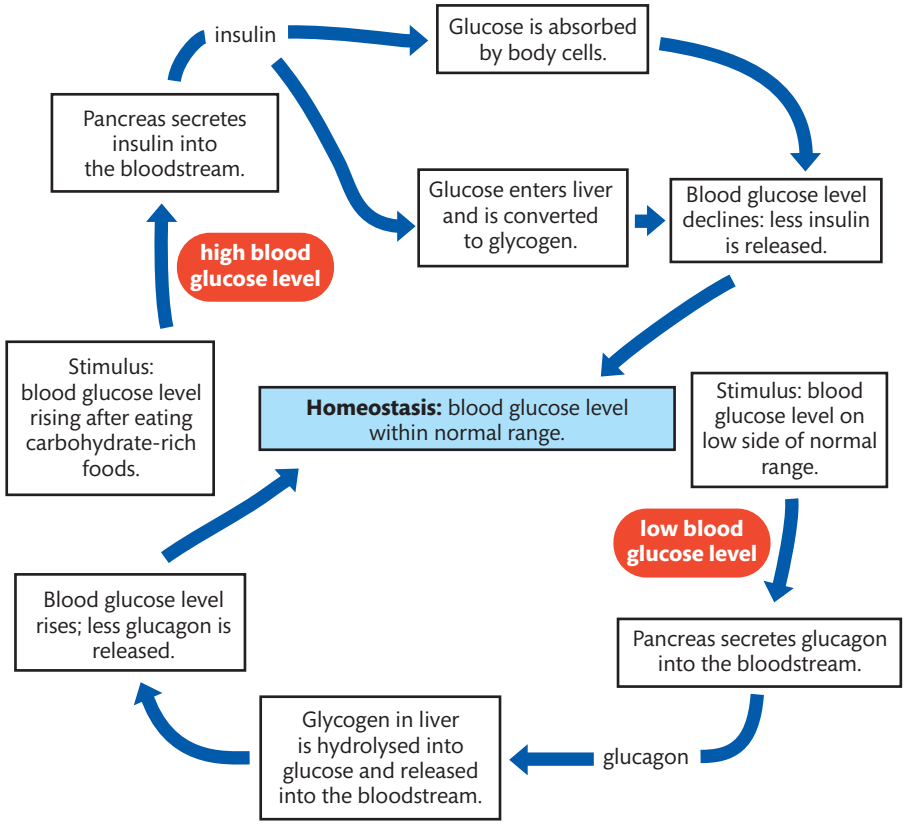


Figure 6.23 Negative feedback control of blood glucose level.

An endocrinologist is a physician who specializes in disorders associated with one or more hormones that are either under-produced (hyposecretion) or over-produced (hypersecretion). Hormone therapy is a branch of medicine that attempts to correct resulting disorders. Common examples are insulin for diabetes, melatonin for sleep disorders, and reproductive hormones following female menopause.

Diabetes

Diabetes is a disease characterized by hyperglycaemia (high blood glucose). Type I is typically caused when the β cells of the pancreas do not produce sufficient insulin; type II diabetes is caused by body cell receptors that do not respond properly to

insulin. You will recall that the hormone insulin should result in increased facilitated diffusion of glucose (through channels) into almost all body cells. This diffusion into body cells lowers the amount of glucose in the bloodstream. People who have untreated diabetes have sufficient glucose in their blood, but not in their body cells where it is needed.

Type I diabetes is controlled by the injection of insulin at appropriate times. Type II diabetes is controlled by diet. Uncontrolled diabetes of either type can lead to many serious effects, including:

- damage to the retina, leading to blindness
- kidney failure
- nerve damage
- increased risk of cardiovascular disease
- poor wound healing (and possibly gangrene, thus making amputation necessary).

Type I diabetes is an autoimmune disease. The body's own immune system attacks and destroys the β cells of the pancreas so that little or no insulin is produced by individuals with type I diabetes. Less than 10% of diabetics have this type of the disease. Type I diabetes most often develops in children or young adults, but can develop in people of any age.

The top three countries for the number of people with diabetes are: (1) China (more than 90 million); (2) India (more than 60 million); (3) USA (more than 23 million).

Type II diabetes is the result of body cells no longer responding to insulin as they once did. This is known as insulin resistance. Initially, the pancreas continues to produce a normal amount of insulin, but this level may decrease after a period of time. Type II diabetes is the most common form of diabetes; approximately 90% of diabetics have this type. Type II diabetes is often associated with genetic history, obesity, lack of exercise and advanced age, and is more common in certain ethnic groups.

Human reproduction

Despite all of the cultural 'trappings' that societies incorporate into the process of human reproduction, it is basically a male gamete (sperm) fertilizing a female gamete (egg or ovum). This cellular union ensures that half of the genetic makeup of the resulting zygote is derived from each parent. Thus, like all forms of sexual reproduction, reproduction in humans serves the bigger purpose of ensuring genetic variation in the species. In both sexes, hormones play a key role in both the development of sexual dimorphism (different body forms of males and females) and the regulation of sexual physiology.

For example, in males the hormone testosterone:

- determines the development of male genitalia during embryonic development
- ensures the development of secondary sex characteristics during puberty
- ensures sperm production as well as maintains sex drive following puberty.

The structures of the male and female reproductive system are adapted for the production and release of the gametes. In addition, the female reproductive system ensures a suitable location for fertilization and provides an environment for the growth of the embryo/foetus until birth.

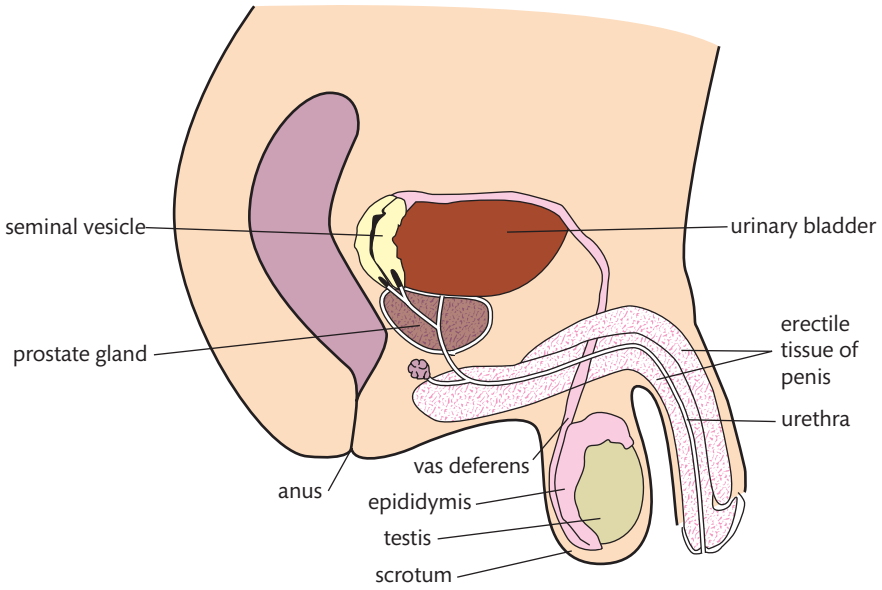
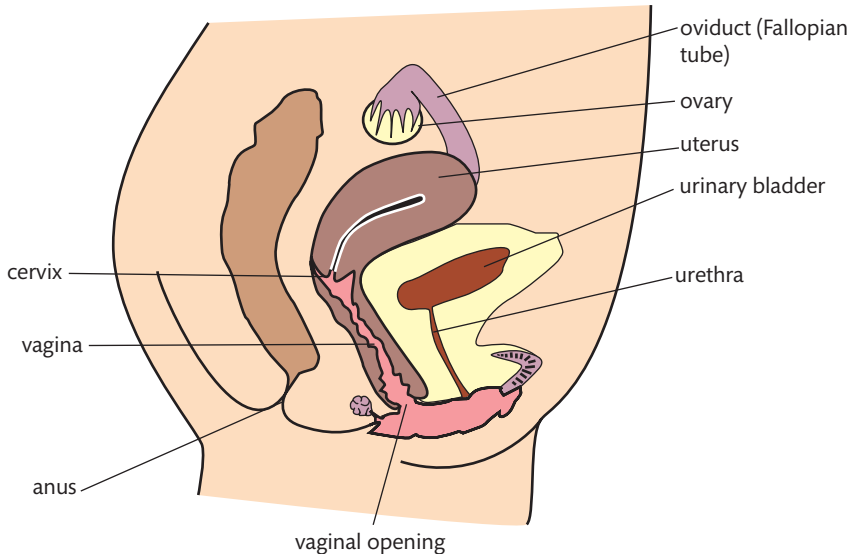


Figure 6.24 Male reproductive system (plus bladder).

Table 6.5 The male reproductive anatomy and function

Male structure	Function(s)
Testis	The male gonads: the sperm are produced here in small tubes called seminiferous tubules
Epididymis	The area where sperm are received, become mature, and are capable of swimming motion via movement of their flagella
Scrotum	Sacs that hold the testes outside the body cavity so that sperm production and maturation can occur at a temperature cooler than body temperature
Vas deferens	A muscular tube that carries mature sperm from the epididymis to the urethra during an ejaculation
Seminal vesicles	Small glands that produce and add seminal fluid to the semen
Prostate gland	A gland that produces much of the seminal fluid, including carbohydrates for the sperm
Penis	An organ that becomes erect as a result of blood engorgement in order to facilitate ejaculation
Urethra	After all the glands have added fluids, this is the tube via which the semen leaves the penis



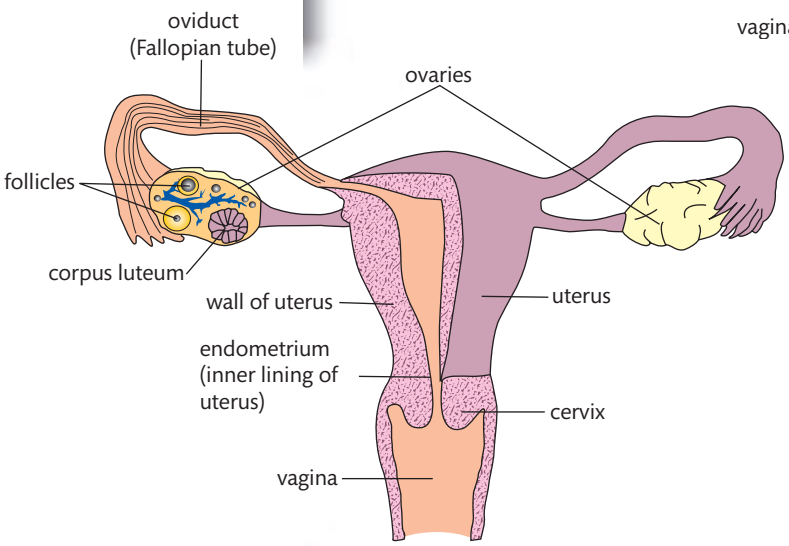


Figure 6.25 Female reproductive system from sagittal (top) and frontal (bottom) views.

Table 6.6 The female reproductive anatomy and function

Female structure	Function(s)
Ovaries	Organs that produce and secrete oestrogen. They also produce and release the ovum (in the form of secondary oocytes). The area where ovulation occurs grows into the corpus luteum, which temporarily produces the hormone progesterone
Fallopian tubes (oviducts)	Ducts that carry the ovum (or early embryo) to the uterus
Uterus	A muscular structure where the early embryo implants and develops if a pregnancy occurs
Endometrium	The highly vascular inner lining of the uterus
Cervix	The lower portion of the uterus, which has an opening to the vagina that allows the sperm to enter for fertilization and provides a pathway for childbirth
Vagina	A muscular tube that leads from the external genitals to the cervix; semen is ejaculated here during sexual intercourse

How does a person become male or female?

You will learn (or have already learnt) that the genetics of becoming male or female depends on whether you inherit an X or a Y chromosome from your father. Because your mother has two X chromosomes, an ovum can only contain an X chromosome. One half of all sperm cells contains an X and one half contains a Y chromosome. If a sperm cell containing an X chromosome fertilizes an ovum, a female is produced. Conversely, if a sperm cell containing a Y chromosome fertilizes an ovum, a male is produced.

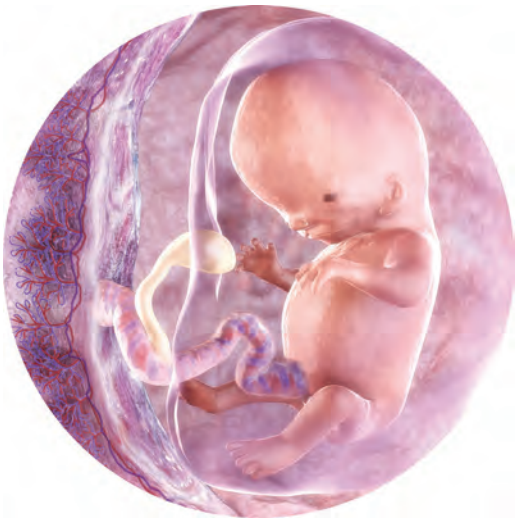
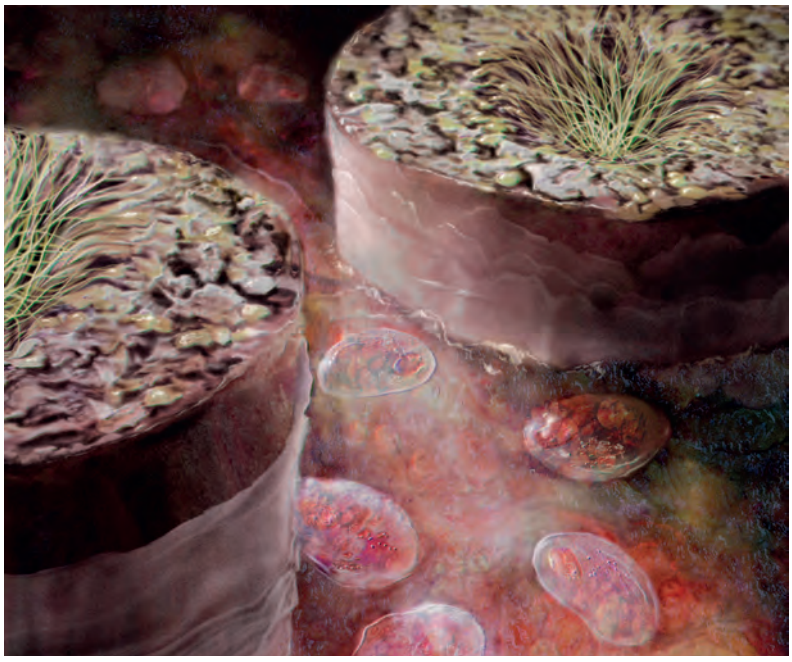


Illustration of a human 8-week-old embryo. The development of internal and external structures characteristic of the sex of the embryo begin about this time. A portion of the placenta is shown on the left, with the umbilical blood vessels within the umbilical cord stretching from the placenta to the embryo.

So, what happens as a result of the XX or XY combinations? The answer lies in the hormones that are produced by each embryo. Embryos of both sexes are virtually identical until about the eighth week following fertilization. Alleles that interact on both of the X chromosomes of female embryos then result in relatively high oestrogen and progesterone production, resulting in the prenatal development of female reproductive structures. Genes located on the single Y chromosome are responsible for early testes development and relatively high testosterone production, resulting in male reproductive structures during subsequent foetal development. It is interesting to note that the male and female reproductive structures have common origins in the pre-8-week-old embryo. In other words, the same embryonic tissue that becomes the ovaries gives rise to the testes, the same embryonic tissue that gives rise to the clitoris gives rise to portions of the penis, etc. Another way of expressing this is to say that some female and male reproductive structures are homologous.



Leydig cells in each testis produce testosterone. Leydig cells are found between the small tubules (seminiferous tubules) that produce spermatozoa (sperm cells). Two seminiferous tubules are shown in cross-section on the upper and left parts of the figure, with Leydig cells in between. Inside the seminiferous tubules you can see developing spermatozoa with flagella surrounded by cells in various stages of meiosis..

It was once assumed that embryos that produced testosterone changed from the 'default' sex of female to male. There is now evidence that each sex requires the influence of specific hormones in order to follow its pathway.

TOK

How much influence should a government have on family planning? A good example of government influence is the One Child Policy of the People's Republic of China. Some, but not all, couples are fined for having more than one child. The policy has had reasonable success as a population control measure, but is resulting in a disproportionately high percentage of males in certain areas of China.

Although males typically experience a lower sperm count as they age, fertility has been documented in men as old as 94 years.

NATURE OF SCIENCE

In Section 6.2 you learnt about the work of William Harvey and how he provided the first valid explanation of how blood circulates in the body. William Harvey was also responsible for much of the early knowledge of a branch of biology that we now call embryology. Embryology is the study of the early development of embryos from fertilized egg to birth. William Harvey's insights were considerable, but lacked information about the earliest embryonic development stages. This was because William Harvey carried out his studies before the microscope had been invented. William Harvey died 17 years before the invention of the microscope.

Role of sex hormones during puberty

When females and males reach puberty, the same hormones that first determined their physical sex are produced and secreted in higher amounts. The increased production of hormones at this time results in the secondary sex characteristics (the attributes that are characteristic of a sex that only appear at puberty).

The secondary sex characteristics of females that arise as a result of increased oestrogen and progesterone production at puberty are:

- enlargement of breasts
- growth of pubic and underarm hair
- widening of hips.

The secondary sex characteristics of males that arise as a result of increased testosterone production at puberty are:

- growth of facial, underarm, chest, and pubic hair
- enlargement of the larynx and associated deepening of the voice
- increased muscle mass
- enlargement of the penis.

The menstrual cycle

Starting at puberty, human females begin a hormonal cycle known as the menstrual cycle. Each cycle lasts, on average, 28 days. The purpose of the menstrual cycle is to time the release of an egg or ovum (ovulation) for possible fertilization and later implantation into the inner lining of the uterus. This implantation must occur when the uterine inner lining (the endometrium) is rich with blood vessels (i.e. highly vascular). The highly vascular endometrium is not maintained if there is no implantation. The breakdown of the blood vessels of the endometrium leads to the menstrual bleeding (menstruation) of a typical cycle. This menstruation is a sign that no pregnancy has occurred.

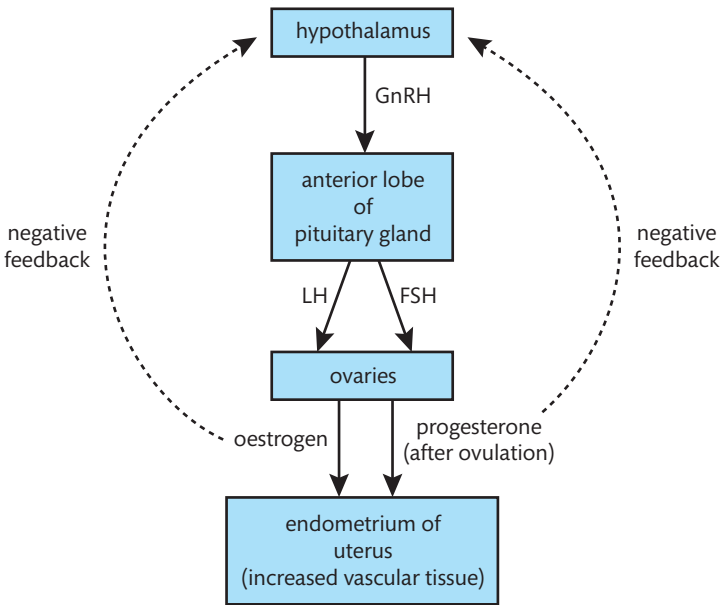


Figure 6.26 Hormonal summary of the menstrual cycle.

Hormones from the hypothalamus and pituitary gland

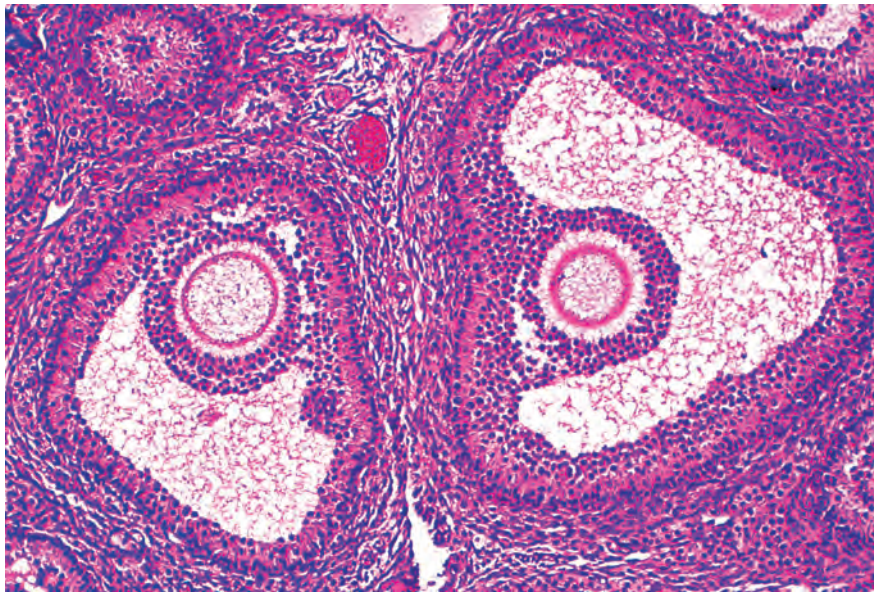
A part of a female's brainstem known as the hypothalamus is the regulatory centre of the menstrual cycle. The hypothalamus produces a hormone known as gonadotropin-releasing hormone (GnRH). The target tissue of GnRH is the nearby pituitary gland, and it results in the anterior pituitary producing and secreting two hormones into the bloodstream. These two hormones are follicle-stimulating hormone (FSH) and luteinizing hormone (LH). The target tissues for these two hormones are the ovaries.

The effects of FSH and LH on the ovaries

The hormones FSH and LH have several effects on the ovaries. One of these effects is to increase the production and secretion of another reproductive hormone by the follicle cells of the ovary. This hormone is oestrogen. Like all hormones, oestrogen enters the bloodstream. Its target tissue is the endometrium of the uterus. One effect of oestrogen is an increase in the density of blood vessels of the endometrium, that is, as stated earlier, the endometrium becomes highly vascular. Another effect of oestrogen is to stimulate the pituitary gland to release more FSH and LH. This is the positive feedback loop of the menstrual cycle, specifically these two sets of hormones increasing because of the increase of the other(s).

Another effect of FSH and LH is the production of structures within the ovaries known as Graafian follicles. Within the ovaries are cells known as follicle cells, and the true reproductive cells that are at a stage of development called oocytes. Under the chemical stimulation of FSH and LH, the somewhat randomly arranged follicle cells and oocytes take on a cellular arrangement known as a Graafian follicle.

A spike in the level of FSH and LH leads to ovulation (the release of the oocyte from the Graafian follicle). The oocyte is accompanied by the inner ring of follicle cells of the Graafian follicle. This entire structure is known as a follicle, and typically enters the Fallopian tube soon after ovulation. The outer ring of follicle cells remains within the ovary. These follicle cells begin to produce and secrete another hormone, progesterone. The cells of this outer ring begin to divide and fill in the 'wound' area left by ovulation, and



A light micrograph showing a human ovary section. Two Graafian follicles are visible, with an oocyte at the centre of each (two inner circles).

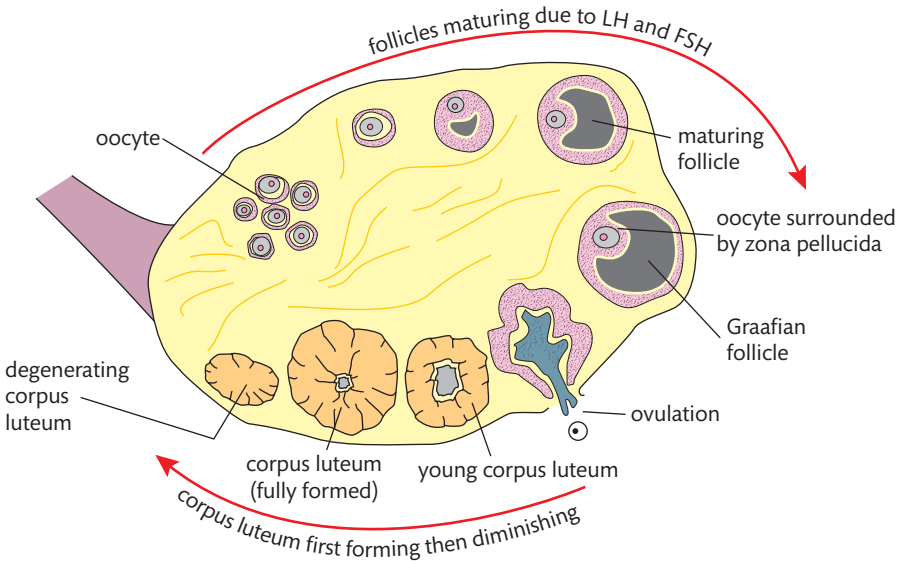


Figure 6.27 Ovary events during a single menstrual cycle. Twenty-eight days of ovarian events are being shown with a single ovary as if in time lapse.

Birth control pills contain both oestrogen and progesterone. Because these pills keep the levels of these two hormones high in a woman's bloodstream, the hypothalamus does not produce GnRH. Thus the pituitary does not produce FSH and LH, and no new Graafian follicles are produced within the ovaries. The end result is that ovulation does not occur.

this forms a glandular structure known as the corpus luteum. The corpus luteum will be hormonally active (producing progesterone) for only 10–12 days after ovulation. Progesterone is a hormone that maintains the thickened, highly vascular endometrium. As long as progesterone continues to be produced, the endometrium will not break down and an embryo will still be able to implant. In addition, the high levels of both oestrogen and progesterone at the same time provide a negative feedback signal to the hypothalamus. The hypothalamus does not produce GnRH when the oestrogen and progesterone levels are high, so FSH and LH remain at levels that are not conducive to the production of another Graafian follicle during this time.

Assuming there is no pregnancy, the corpus luteum begins to break down after 10–12 days, and this leads to a decline in both progesterone and oestrogen levels. As both of these hormone levels fall, the highly vascular endometrium can no longer be maintained. The capillaries and small blood vessels begin to rupture and menstruation begins. The drop in progesterone and oestrogen also signals the hypothalamus to begin secreting GnRH, and thus another menstrual cycle begins. Because the menstrual cycle is a cycle, there is no true beginning or ending point. The first day of menstruation is designated as the first day of the menstrual cycle simply because this is an event that can be easily discerned (see Figure 6.28).

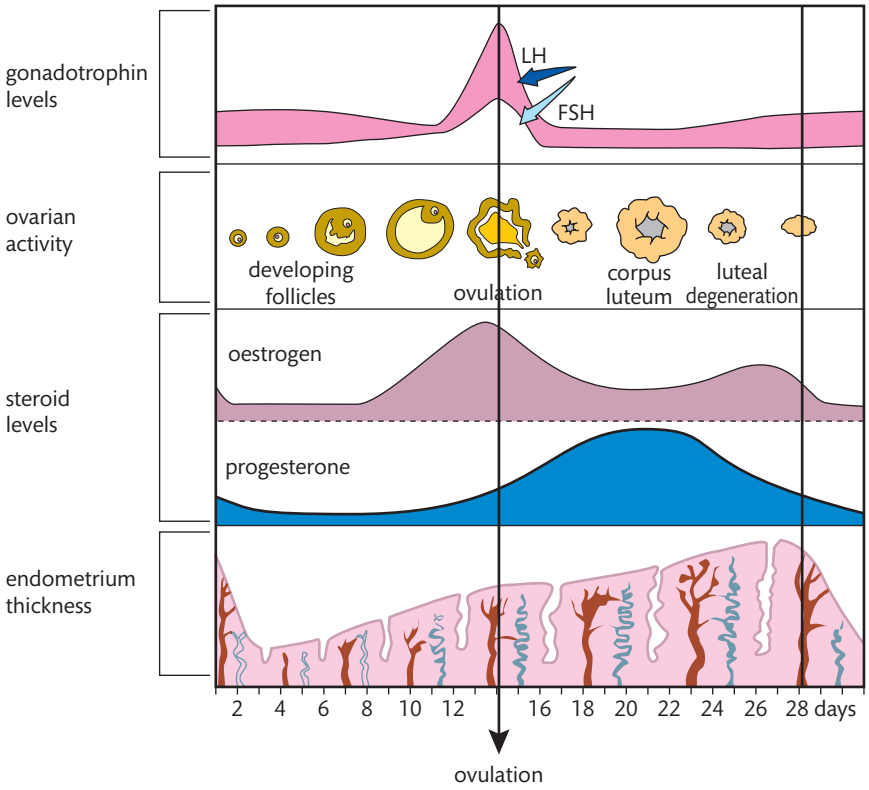


Figure 6.28 Events occurring during a 28-day menstrual cycle. Note that these events are all aligned on the same time scale. Ovulation and possible fertilization occur near the middle of the cycle.

When making sense of Figure 6.28, use the line indicating the time of ovulation as an important marker. Ask yourself: 'What events led up to and resulted in this ovulation?' and 'What will now happen after ovulation?'

In vitro fertilization (IVF)

Natural fertilization typically occurs in one of a female's Fallopian tubes 24–48 hours after ovulation. The resulting zygote begins to divide by mitosis, and takes several more days to travel down the Fallopian tube to the endometrium of the uterus. When the embryo reaches the endometrium, it has already divided mitotically many times and is a ball of about 100 cells. The embryo, called a blastocyst at this stage, will then implant in the highly vascular tissue of the endometrium.

Some couples are unable to bear children. There is a wide variety of possible reasons for infertility, including:

- males with low sperm counts
- males with impotence (failure to achieve or maintain an erection)
- females who cannot ovulate normally
- females with blocked Fallopian tubes.

Reproductive technologies have been developed to help overcome these situations. One of the most common of these new technologies is *in vitro* fertilization (IVF).

Hormone therapy

As part of the IVF procedure, a woman must have eggs 'harvested' from her ovaries. In order to ensure the proper timing for this, and to maximize the number of available ova, the woman undergoes about a month of hormone therapy. During the first 2 weeks she injects a drug (or uses a nasal spray of the drug) that suspends her own natural hormones associated with her menstrual cycle. Then for the next 12 days or so she takes hormone injections that include FSH. This ensures that she will produce many Graafian follicles in each ovary and provide many potential ova (oocytes) for harvesting. The production of many more eggs than is typical of a normal menstrual cycle is called superovulation.

When the time is right, several eggs (oocytes) are then harvested surgically. To obtain the sperm cells that are needed for fertilization, the man ejaculates into a container. Harvested eggs are mixed with the sperm cells in separate culture dishes. Microscopic observation reveals which ova are fertilized, and whether the early development appears normal and healthy. Between one and three healthy embryos are later introduced into the woman's uterus for implantation. Any healthy embryos from the culturing phase that are not implanted can be frozen and used later if another implantation procedure is needed.

TOK

Screening the embryos used in IVF for certain genetic conditions is becoming a common practice. Screening for desirable traits is possible, and may soon become a routine part of the IVF procedures offered by medical clinics. How much will the course of human evolution be effected by such screening practices?

NATURE OF SCIENCE

Always consider the source! If you do a web search for IVF, many of the sites you will encounter will be from private clinics that offer IVF as a paid service. This doesn't mean the information on those sites is incorrect, but it does mean you need to consider the possible bias behind the information.

Exercises

17 If possible, without looking back though this chapter, give a very brief description of the function of each of these hormones: insulin, glucagon, thyroxin, leptin, and melatonin.

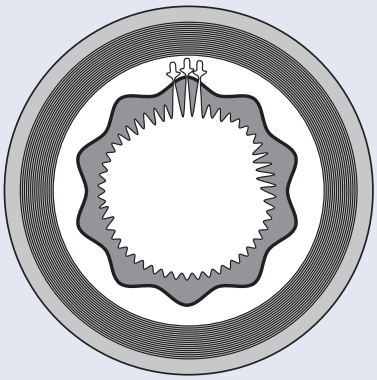
18 What is an example of a positive feedback loop in the menstrual cycle?

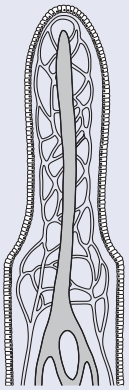
19 What is an example of a negative feedback loop in the menstrual cycle?

To learn more about this chapter, go to the hotlinks site, search for the title or ISBN and click on Chapter 6.

Practice questions

1 The first figure shows a cross-section through the small intestine, and the second figure shows an enlarged longitudinal section through a single villus.





Using these diagrams, outline **three** ways in which the structure of the small intestine is related to its function of absorbing food.

(*Total 3 marks*)

2 Draw a diagram of the human digestive system.

(*Total 4 marks*)

3 Explain the relationship between the structure and function of arteries, veins, and capillaries.

(*Total 9 marks*)

4 Explain why antibiotics are effective against bacteria but not viruses.

(*Total 3 marks*)

5 A blood clot contains a network of protein. What is the protein?

A Fibrin

B Fibrinogen

C Haemoglobin

D Thrombin

(*Total 1 mark*)

6 What happens during inhalation?

A Both the external intercostal muscles and the diaphragm contract.

B The internal intercostal muscles contract and the diaphragm relaxes.

C The external intercostal muscles relax and the diaphragm contracts.

D Both the internal intercostal muscles and the diaphragm relax.

(*Total 1 mark*)

7 Describe the principles of synaptic transmission in the nervous system.

(*Total 6 marks*)